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     FILE 'HCAPLUS' ENTERED AT 14:43:42 ON 04 AUG 2004
L1            1 US20040038999/PN

     FILE 'REGISTRY' ENTERED AT 14:44:00 ON 04 AUG 2004

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L2              TRA L1 1- RN :       37 TERMS

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L3           37 SEA L2

     FILE 'WPIX' ENTERED AT 14:44:09 ON 04 AUG 2004
L4            1 US20040038999/PN

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FILE LAST UPDATED: 3 Aug 2004  (20040803/ED)

 This file contains CAS Registry Numbers for easy and accurate
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'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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L1   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:143149  HCAPLUS
DN   140:199338
ED   Entered STN:  22 Feb 2004
TI   Preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors
IN   Goldstein, David Michael; Lim, Julie Anne
PA   F. Hoffmann-La Roche Ag, Switz.
SO   PCT Int. Appl., 55 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  C07D471-04
     ICS  A61K031-519; A61P029-00
CC   28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
     Section cross-reference(s): 1, 63
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FAN.CNT 1

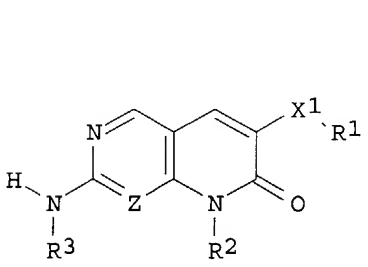
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004014907	A1	20040219	WO 2003-EP8357	20030729
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004038999	A1	20040226	US 2003-634936	20030805 <--
PRAI	US 2002-401491P	P	20020806		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004014907	ICM	C07D471-04
	ICS	A61K031-519; A61P029-00

OS MARPAT 140:199338

GI



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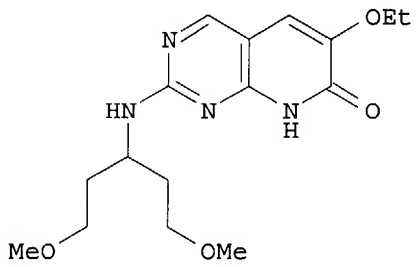

II

AB The title compds. [I; R1 = alkyl, cycloalkyl, cycloakylalkyl, or CH2(alkenyl); X1 = O, NH, N(alkyl), S, CO; Z = N, CH; R2 = H, alkyl, cycloalkyl, etc.; R3 = alkyl, haloalkyl, aryl, etc.], were prepared E.g., a 3-step synthesis of II (starting from 4-amino-2-butylsulfanyl-4,5-dihydropyrimidine-5-carboxaldehyde and Et ethoxyacetate) which showed IC50 of about 7.7 .mu.M in p38 MAP kinase in vitro assay, was given. The pharmaceutical composition comprising the compound I is claimed.

ST alkoxypyridopyrimidine prepn p38 MAP kinase inhibitor; pyridopyrimidine alkoxy prepn p38 MAP kinase inhibitor

IT Intestine, disease
(Crohn's, treatment of; preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT Respiratory distress syndrome
(adult, treatment of; preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT Spinal column, disease
(ankylosing spondylitis, treatment of; preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT Lung, disease
(chronic obstructive, treatment of; preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT Intestine, disease

(inflammatory, treatment of; preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT Intestine, disease
(irritable bowel syndrome, treatment of; preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT Anti-Alzheimer's agents
Anti-inflammatory agents
Antiasthmatics
Antirheumatic agents
Human
(preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT Arthritis
(psoriatic arthritis, treatment of; preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT Alzheimer's disease
Asthma
Psoriasis
Rheumatoid arthritis
(treatment of; preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT 165245-96-5, p38 MAP kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT 661450-66-4P 661450-67-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT 661450-62-0P 661450-63-1P 661450-64-2P 661450-65-3P 661450-68-6P 661450-69-7P 661450-70-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT 817-95-8, Ethyl ethoxyacetate 2032-34-0, 3,3-Diethoxypropanenitrile 5909-24-0, Ethyl 4-chloro-2-methylthiopyrimidine-5-carboxylate 6290-49-9, Methyl methoxyacetate 28177-48-2, 2,6-Difluorophenol 38041-19-9, 4-Aminotetrahydropyran 58859-46-4, Ethyl 4-amino-1-piperidinecarboxylate 661450-77-7 661450-78-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

IT 770-31-0P, 4-Amino-2-(methylthio)pyrimidine-5-carboxaldehyde 17759-30-7P, 4-Methylamino-2-methylthiopyrimidine-5-methanol 76360-82-2P, Ethyl 4-(methylamino)-2-(methylthio)pyrimidine-5-carboxylate 102669-01-2P 105161-35-1P 185040-32-8P, 4-Methylamino-2-methylthiopyrimidine-5-carboxaldehyde 185040-33-9P 185040-34-0P 185040-35-1P, 4-Ethylamino-2-methylthiopyrimidine-5-carboxaldehyde 449808-49-5P 449810-42-8P 449811-11-4P 661450-71-1P 661450-72-2P 661450-73-3P 661450-74-4P 661450-75-5P 661450-76-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Bartolome, A; US 2002055513 A1 2002 HCAPLUS
(2) La Roche, H; WO 0129041 A 2001 HCAPLUS
(3) Switz; WO 02064594 A 2002 HCAPLUS
(4) Warner-Lambert Company; WO 03062236 A 2003 HCAPLUS

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FILE LAST UPDATED:          2 AUG 2004      <20040802/UP>
MOST RECENT DERWENT UPDATE:     200449        <200449/DW>
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=> d all l4

L4   ANSWER 1 OF 1  WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN   2004-238720 [22]   WPIX
DNC  C2004-093381
TI   New 2,6-disubstituted 7-oxo-pyrido(2,3-d)pyrimidines useful for the
     treatment of p38 mediated disorder e.g. rheumatoid arthritis.
DC   B02
IN   GOLDSTEIN, D M; LIM, J A
PA   (GOLD-I) GOLDSTEIN D M; (LIMJ-I) LIM J A; (HOFF) HOFFMANN LA ROCHE & CO AG
     F
CYC  103
PI   WO 2004014907   A1 20040219 (200422)* EN   53    C07D471-04
        RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
            LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
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            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
            RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA
            ZM ZW
     US 2004038999   A1 20040226 (200422)              A61K031-519    <--
ADT  WO 2004014907 A1 WO 2003-EP8357 20030729; US 2004038999 A1 Provisional US
     2002-401491P 20020806, US 2003-634936 20030805
PRAI US 2002-401491P      20020806; US 2003-634936       20030805
IC   ICM  A61K031-519; C07D471-04
```

ICS A61P029-00; C07D471-02; C07D487-02

AB WO2004014907 A UPAB: 20040331

NOVELTY - 2,6-Disubstituted 7-oxo-pyrido(2,3-d)pyrimidines are new.

DETAILED DESCRIPTION - 2,6-Disubstituted 7-oxo-pyrido(2,3-d)pyrimidines of formula (I), their salts, hydrates or prodrugs are new.

Z = N or CH;

X1 = O, NR4, S or C(O);

R4 = H or alkyl;

R1 = T1, alkenylene or -CH2-alkenyl;

T1 = (cyclo)alkyl, cycloalkylalkyl;

R2 = H, T1, aryl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, alkylene-C(O)-R21, amino, monoalkylamino, dialkylamino, acyl or NR22-Y-R23;

R21 = H, alkyl OH, alkoxy, amino, monoalkylamino or dialkylamino;

Y = -C(O), -C(O)O-, -C(O)NR24, S(O)2 or S(O)2NR25;

R22, R24 and R25 = H or alkyl;

R23 = H, T1, heteroalkyl or optionally substituted phenyl;

R3 = H, haloalkyl, (hetero)aryl, (hetero)aralkyl, T1, heteroalkyl substituted cycloalkyl, hetero-substituted cycloalkyl, heteroalkyl, cyanoalkyl, heterocyclyl, heterocyclylalkyl, or -heterocycloamino-SO2-R12; and

R12 = haloalkyl, (hetero)aryl, arylalkyl or heteroaralkyl.

INDEPENDENT CLAIMS are included for the following:

(1) preparation of (I); and

(2) use of (I) in the manufacture of medicament for the treatment of a p38 mediated disorder e.g. rheumatoid arthritis.

ACTIVITY - Antiarthritic; Antirheumatic; Antipsoriatic; Antiinflammatory; Gastrointestinal-Gen.; Respiratory-Gen.; Antiasthmatic; Neuroprotective; Nootropic; Immunosuppressive; Ophthalmological; Dermatological; Cardiovascular-Gen.; CNS-Gen.; Antidiabetic; Antipyretic; Antigout; Osteopathic; Virucide; Antibacterial; Antimalarial; Immunomodulator; Anti-HIV; Vasotropic; Antiarteriosclerotic; Thrombolytic; Anticoagulant; Cardiant; Nephrotropic; Hepatotropic; Vulnerary; Antiulcer; Uropathic; Cytostatic; Antiangiogenic; Gynecological.

MECHANISM OF ACTION - p38-(Mitogen-activated protein kinases (MAP))kinase inhibitor; LPS-induced TNF- alpha -production inhibitor.

An in vitro assay of p38(MAP)kinase was evaluated as follows: p-38 MAP kinase inhibitory activity of hydrochloride of 6-ethoxy-8-methyl-2-(((1-methanesulfonyl)piperidinyl-4-yl)amino)pyrido(2,3-d)pyrimidin-7(8H)one (Ia) was determined by measuring the transfer of the gamma -phosphate form gamma -33P-ATP by p-38 kinase to Myelin Basic Protein (MBP) using minor modification of the method described in Ahn et al., J. Biol. Chemical, 266:4220-4227(1991). The phosphorylated p38 MAP kinase was diluted in kinase buffer (containing 3-(N-morpholino)propanesulfonic acid (20 mM), pH 7.2, beta -glycerol phosphate (25 mM), ethylene glycol-bis(beta -aminoethyl ether)-N,N,N',N'-tetraacetic acid (5 MM), sodium ortho-vandate (1 mM), dithiothreitol (1 mM), magnesium chloride (40 mM)). The test compound dissolved in dimethylsulfoxide (DMSO) or only DMSO (control) was added and the samples were incubated for 10 minutes at 30 deg. C. After incubation, for an additional 20 minutes at 30 deg. C, the reaction was terminated by adding phosphoric acid (0.75%) followed by separation of residual gamma -33P-ATP. The IC50 value of the test compound was found to be approx. 0.058 micro M.

USE - As active substances for the manufacture of medicament for the treatment of a p38 mediated disorder e.g. rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, Crohn's disease, irritable bowel syndrome, inflammatory bowel disease, psoriasis, adult respiratory distress syndrome, asthma or chronic obstructive pulmonary disease, Alzheimer's disease (all claimed). Also useful for the treatment or prophylaxis of inflammatory, immunological, oncological, bronchopulmonary,

dermatological and cardiovascular disorders; in the treatment of central nervous system disorders or diabetic complications or for the prevention of graft rejection following transplant surgery; for the treatment of inflammation in a subject; as antipyretics for the treatment of fever, arthritis (including spondyloarthropathies), gouty arthritis, psoriatic arthritis, osteoarthritis, systemic lupus erythematosus, juvenile arthritis, and other arthritic conditions; for the treatment of pulmonary disorders or lung inflammation (including adult respiratory distress syndrome, pulmonary sarcoidosis, asthma, silicosis, and chronic pulmonary inflammatory disease; for the treatment of viral and bacterial infections (including sepsis, septic shock, gram negative sepsis, malaria, meningitis, cachexia secondary to or malignancy, cachexia secondary to AIDS, ARC (AIDS related complex), pneumonia, and herpes virus; for the treatment of bone resorption diseases (such as osteoporosis, endotoxic shock, toxic shock syndrome, reperfusion injury, autoimmune disease (including graft versus host reaction and allograft rejections), cardiovascular diseases (including atherosclerosis, thrombosis, congestive heart failure, and cardiac reperfusion injury, renal reperfusion injury, liver disease and nephritis, and myalgias due to infection); for the treatment of Alzheimer's disease, influenza, multiple sclerosis, cancer, diabetes, systemic lupus erythematosus (SLE), skin-related conditions (such as psoriasis, eczema, burns, dermatitis, keloid formation, and scar tissue formation; for treating gastrointestinal conditions (such as gastritis and ulcerative colitis); in the treatment of ophthalmic disease (such as retinitis, retinopathies, uveitis, ocular photophobia, and of acute injury to the eye tissue); in treating angiogenesis (including neoplasia, metastasis; ophthalmological conditions (such as corneal graft rejection, ocular neovascularization, retinal neovascularization (including neovascularization following injury or infection, diabetic retinopathy, retrolental fibroplasia and neovascular glaucoma; ulcerative diseases such as gastric ulcer; pathological, but non-malignant, conditions such as hemangiomas (including infantile hemangiomas, angiofibroma of the nasopharynx and avascular necrosis of bone); diabetic nephropathy and cardiomyopathy; and disorders of the female reproductive system such as endometriosis; for the treatment of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, Crohn's disease, irritable bowel syndrome, inflammatory bowel disease, psoriasis, adult respiratory distress syndrome, asthma or chronic obstructive pulmonary disease or Alzheimer's disease or oncological disorders; for veterinary treatment of companion animals, exotic animals and farm animals (including mammals or rodents).

ADVANTAGE - (I) possess the desired pharmacological activity.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B06-D06; B06-D08; B14-A01; B14-A02; B14-A03B; B14-C03; B14-C04; B14-C06; B14-C09; B14-D07C; B14-E08; B14-E10B; B14-E10C; B14-E11; B14-F01; B14-F02; B14-F04; B14-F05; B14-F07; B14-G01; B14-G02; B14-G03; B14-H01; B14-J01A4; B14-K01; B14-N01; B14-N03; B14-N10; B14-N12; B14-N14; B14-N16; B14-N17; B14-S01; B14-S04; B14-S06; B14-S12

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DICTIONARY FILE UPDATES:    3 AUG 2004  HIGHEST RN 721883-12-1

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L5                STR
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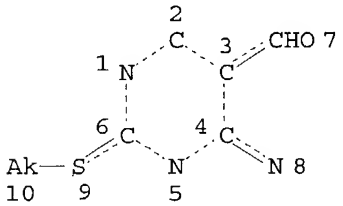


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   1
NUMBER OF NODES IS  10

STEREO ATTRIBUTES: NONE
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SEARCH TIME: 00.00.01


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L8   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   185040-35-1  REGISTRY
CN   5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI)  (CA
     INDEX NAME)
OTHER NAMES:
CN   4-(Ethylamino)-2-(methylsulfanyl)pyrimidine-5-carboxaldehyde
CN   4-(Ethylamino)-2-(methylthio)pyrimidine-5-carboxaldehyde
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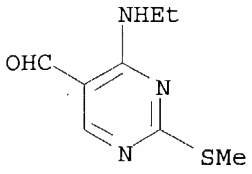
CN 4-Ethylamino-2-methanethiopyrimidine-5-carboxaldehyde
FS 3D CONCORD
MF **C8 H11 N3 O S**
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

15 REFERENCES IN FILE CA (1907 TO DATE)
15 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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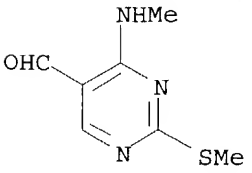
L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 185040-32-8 REGISTRY
CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-(Methylamino)-2-(methylthio)pyrimidine-5-carboxaldehyde
CN 4-Methylamino-2-methanethiopyrimidine-5-carboxaldehyde
FS 3D CONCORD
MF **C7 H9 N3 O S**
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)



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16 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 211247-46-0 REGISTRY
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OTHER NAMES:
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CN 4-Cyclopropylamino-2-methylthiopyrimidine-5-carboxaldehyde
FS 3D CONCORD
MF **C9 H11 N3 O S**
SR CA
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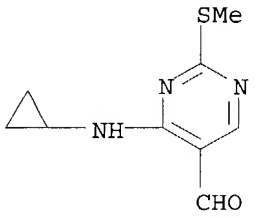
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)



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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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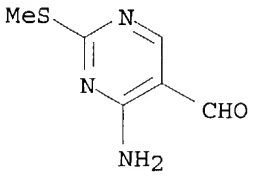
L11 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 770-31-0 REGISTRY
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-Amino-2-(methylthio)pyrimidine-5-carboxaldehyde
CN 4-Amino-2-methanethiopyrimidine-5-carboxaldehyde
CN NSC 165376
FS 3D CONCORD
MF **C6 H7 N3 O S**
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
RL.NP Roles from non-patents: NORL (No role in record)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

21 REFERENCES IN FILE CA (1907 TO DATE)
21 REFERENCES IN FILE CAPLUS (1907 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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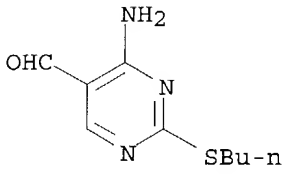
L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **661450-77-7** REGISTRY
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(butylthio)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF **C9 H13 N3 O S**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)



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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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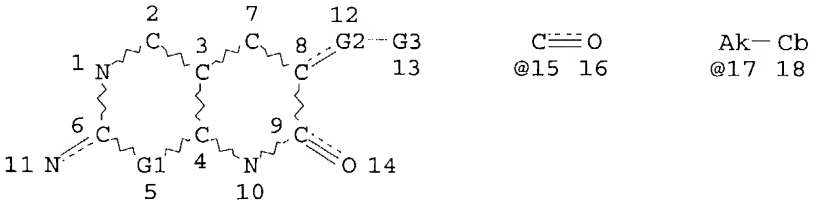

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VAR G3=AK/CB/17
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DEFAULT ECLEVEL IS LIMITED

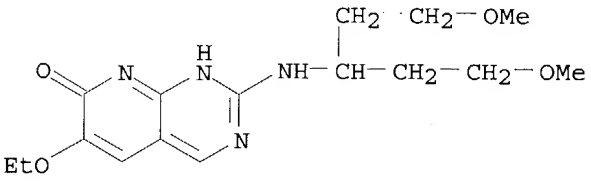
GRAPH ATTRIBUTES:
RSPEC 1
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
L17 297 SEA FILE=REGISTRY SSS FUL L15

100.0% PROCESSED 1504 ITERATIONS 297 ANSWERS
SEARCH TIME: 00.00.01

=> d ide l18

L18 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 661450-62-0 REGISTRY
CN Pyrido[2,3-d]pyrimidin-7(1H)-one, 6-ethoxy-2-[[3-methoxy-1-(2-methoxyethyl)propyl]amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF **C16 H24 N4 O4**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)



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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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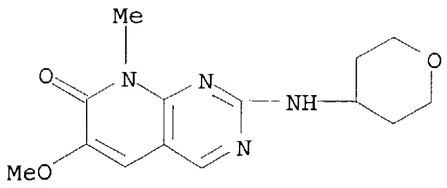
L19 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 661450-64-2 REGISTRY
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-methoxy-8-methyl-2-[(tetrahydro-2H-pyran-4-yl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)
MF **C14 H18 N4 O3 . Cl H**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (661450-63-1)



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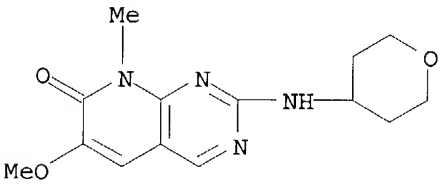
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L19 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 661450-63-1 REGISTRY
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-methoxy-8-methyl-2-[(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF **C14 H18 N4 O3**
CI COM
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)



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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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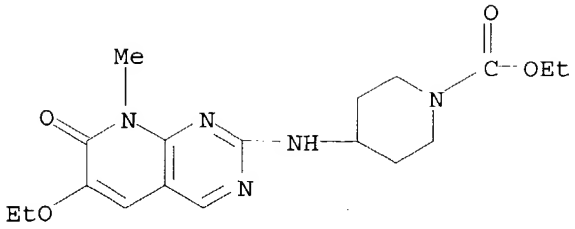
L20 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 661450-67-5 REGISTRY
CN 1-Piperidinecarboxylic acid, 4-[(6-ethoxy-7,8-dihydro-8-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-, ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF **C18 H25 N5 O4**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

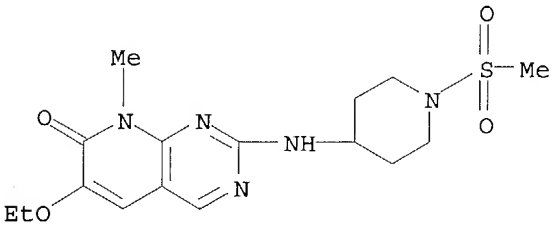


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d ide l22 tot

L22 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 661450-70-0 REGISTRY
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-ethoxy-8-methyl-2-[[1-(methylsulfonyl)-4-piperidinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)
MF **C16 H23 N5 O4 S . Cl H**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (661450-69-7)

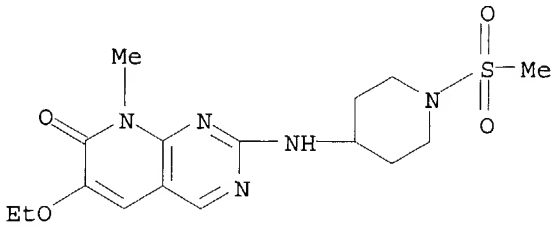


● HCl

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L22 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 661450-69-7 REGISTRY
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-ethoxy-8-methyl-2-[[1-(methylsulfonyl)-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF **C16 H23 N5 O4 S**
CI COM
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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L1 1 US20040038999/PN

FILE 'REGISTRY' ENTERED AT 14:44:00 ON 04 AUG 2004

FILE 'HCAPLUS' ENTERED AT 14:44:05 ON 04 AUG 2004
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FILE 'REGISTRY' ENTERED AT 14:44:05 ON 04 AUG 2004
L3 37 SEA L2

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L4 1 US20040038999/PN

FILE 'REGISTRY' ENTERED AT 15:19:49 ON 04 AUG 2004
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L7 70 L5 FULL
SAVE TEMP NWAO936F1/A L7
L8 1 C8H11N3OS AND L7
L9 1 C7H9N3OS AND L7
L10 1 C9H11N3OS AND L7
L11 1 C6H7N3OS AND L7
L12 2 C9H13N3OS AND L7
SEL RN 1
L13 1 E1 AND L12
L14 STR
L15 STR L14
L16 19 L15
L17 297 L15 FULL
SAVE TEMP L17 NWAO936F2/A
L18 1 C16H24N4O4 AND L17
L19 2 C14H18N4O3 AND L17
L20 1 C18H25N5O4 AND L17

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L22             2 C16H23N5O4S AND L17
L23               STR L15
L24             0 L23 SAM SUB=L17
L25               STR L23
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L27             0 L25 FULL SUB=L17

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L29           200 E3,E11,E40-41,E29
                  E LIM J/AU
L30            72 E3-4
                  E LIM JULIE/AU
L31             6 E3-5
                  E ROCHE PALO/CS
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L33             5 L28 AND L29-31
L34             0 L28 AND L32
L35            29 L28 NOT L33
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                  EDIT E1-E4 /AN /OREF

     FILE 'HCAPLUS' ENTERED AT 16:22:27 ON 04 AUG 2004
L43            10 E1-4
L44            35 L36 OR L43

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L45             0 L17

     FILE 'HCAPLUS' ENTERED AT 16:26:13 ON 04 AUG 2004
L46             0 L44 AND L29-32

=> b hcap
FILE 'HCAPLUS' ENTERED AT 16:31:36 ON 04 AUG 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 4 Aug 2004 VOL 141 ISS 6
FILE LAST UPDATED: 3 Aug 2004 (20040803/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d bib abs fhitstr hitrn l33 tot

L33 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:143149 HCAPLUS
DN 140:199338
TI Preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors
IN **Goldstein, David Michael; Lim, Julie Anne**
PA F. Hoffmann-La Roche Ag, Switz.
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004014907	A1	20040219	WO 2003-EP8357	20030729
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004038999	A1	20040226	US 2003-634936	20030805
PRAI	US 2002-401491P	P	20020806		

OS MARPAT 140:199338
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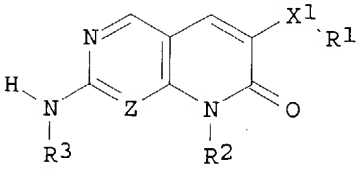

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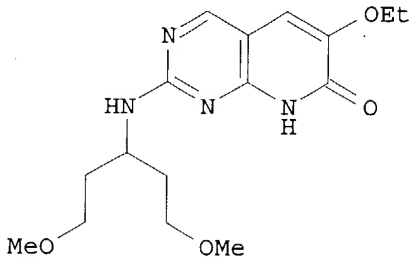
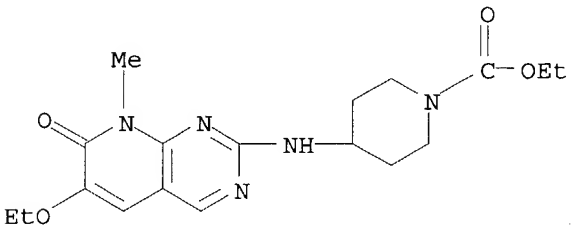


II

AB The title compds. [I; R1 = alkyl, cycloalkyl, cycloakylalkyl, or CH2(alkenyl); X1 = O, NH, N(alkyl), S, CO; Z = N, CH; R2 = H, alkyl, cycloalkyl, etc.; R3 = alkyl, haloalkyl, aryl, etc.], were prepared E.g., a 3-step synthesis of II (starting from 4-amino-2-butylsulfanyl-4,5-dihydropyrimidine-5-carboxaldehyde and Et ethoxyacetate) which showed IC50

of about 7.7 .mu.M in p38 MAP kinase in vitro assay, was given. The pharmaceutical composition comprising the compound I is claimed.

IT **661450-67-5P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)
RN 661450-67-5 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[(6-ethoxy-7,8-dihydro-8-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-, ethyl ester (9CI) (CA INDEX NAME)



IT **661450-67-5P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)
IT **661450-62-0P 661450-63-1P 661450-64-2P**
661450-69-7P 661450-70-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)
IT **661450-77-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)
IT **770-31-0P**, 4-Amino-2-(methylthio)pyrimidine-5-carboxaldehyde **185040-32-8P**, 4-Methylamino-2-methylthiopyrimidine-5-carboxaldehyde **185040-35-1P**, 4-Ethylamino-2-methylthiopyrimidine-5-carboxaldehyde
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 6-alkoxy-pyridopyrimidines as p-38 MAP kinase inhibitors)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:637680 HCAPLUS
DN 137:185502
TI Preparation of 2,6-disubstituted 7-oxopyrido[2,3-d]pyrimidines for treating p38 mediated disorders
IN Chen, Jian Jeffrey; Dunn, James Patrick; **Goldstein, David Michael**; Stahl, Christoph Martin
PA F. Hoffmann-La Roche Ag, Switz.
SO PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 2002064594	A2	20020822	WO 2002-EP1106	20020204
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1361880	A2	20031119	EP 2002-726103	20020204
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	US 6696566	B2	20040224		
	NO 2003003540	A	20030811	NO 2003-3540	20030811
	US 2004116698	A1	20040617	US 2003-722703	20031125
PRAI	US 2001-268375P	P	20010212		
	US 2001-334654P	P	20011130		
	WO 2002-EP1106	W	20020204		
	US 2002-73845	A1	20020211		

OS MARPAT 137:185502

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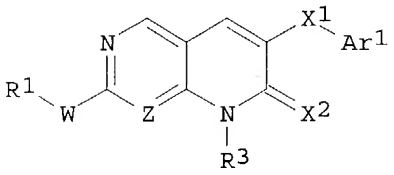

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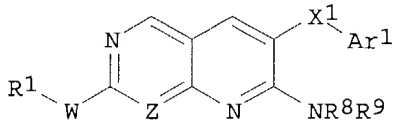

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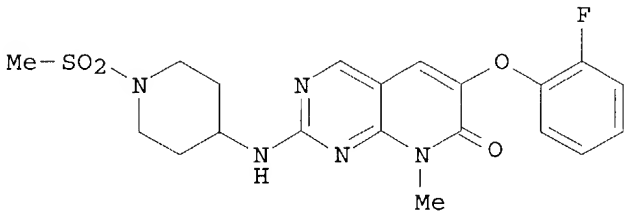


III

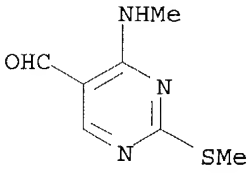
AB The title compds. with general formula I or II [wherein Z = N or CH; W = NR2; X1 = O, NR4, S, CR5R6, or CO; R4, R5, and R6 = independently H or alkyl; X2 = O or NR7; Ar1 = (hetero)aryl; R2 = H, alkyl, acyl, alkoxycarbonyl, aryloxycarbonyl, heteroalkyl(oxy)carbonyl, or R21-R22; R21 = alkylene or CO; R22 = alkyl or alkoxy; R1 = H, (halo)alkyl, (hetero)aryl, (hetero)aralkyl, cyclo(alkyl)alkyl, hetero(cyclyl)alkyl, cyanoalkyl, heterocyclyl, or substituted hetero(alkyl)cycloalkyl, heterocycloamino, or acyl(alkylene); R3 = H, (cyclo)alkyl, cycloalkylalkyl, aryl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, acylalkylene, (un)substituted amino; R7 = H or alkyl; R8 and R9 = independently H, (cyclo)alkyl, aryl(sulfonyl), aralkyl, cycloalkylalkyl, heteroalkyl, alkylsulfonyl, acyl, etc.; and pharmaceutically acceptable salts thereof] were prepared For example, the substitution reaction of

6-(2-fluorophenoxy)-8-methyl-2-(methylsulfonyl)pyrido[2,3-d]pyrimidin-7(8H)-one (preparation given) and 1-(methylsulfonyl)piperidin-4-amine (preparation given), followed by salt formation, gave the phenoxypyrido[2,3-d]pyrimidinone III.bul.HCl. I and II have IC50 activity against p38 kinase in the range of 0.1-5000 nM, with the majority being 1-1000 nM. I and II are useful for the treatment of arthritis, Crohn's disease, irritable bowel syndrome, adult respiratory distress syndrome, chronic obstructive pulmonary disease, or Alzheimer's disease (no data).

IT **185040-32-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of oxopyrido[2,3-d]pyrimidines for treating p38 mediated disorders)

RN 185040-32-8 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



IT **185040-32-8P 185040-35-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of oxopyrido[2,3-d]pyrimidines for treating p38 mediated disorders)

IT **770-31-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of oxopyrido[2,3-d]pyrimidines for treating p38 mediated disorders)

L33 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:171896 HCAPLUS

DN 136:232316

TI 7-Oxopyridopyrimidines as inhibitors of cellular proliferation, and particularly as inhibitors of p38 kinase, for treatment of p38-related conditions

IN Chen, Jian Jeffrey; Dunn, James Patrick; **Goldstein, David Michael**; **Lim, Julie Anne**

PA F. Hoffmann-La Roche Ag, Switz.

SO PCT Int. Appl., 135 pp.
CODEN: PIXXD2

DT Patent

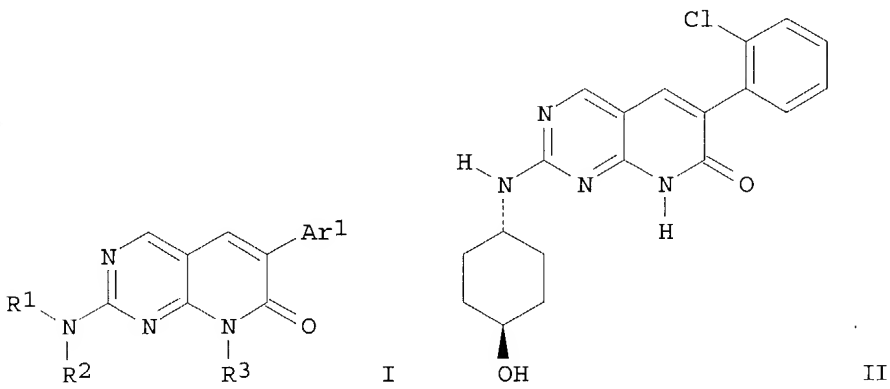
LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002018380	A1	20020307	WO 2001-EP9689	20010822

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001093784	A5	20020313	AU 2001-93784	20010822
	EP 1315726	A1	20030604	EP 2001-974206	20010822
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001013628	A	20030701	BR 2001-13628	20010822
	JP 2004507541	T2	20040311	JP 2002-523895	20010822
	US 2002055513	A1	20020509	US 2001-943338	20010830
	US 6518276	B2	20030211		
	US 2002137756	A1	20020926	US 2001-943407	20010830
	US 6506749	B2	20030114		
	US 2003153586	A1	20030814	US 2002-230723	20020829
	US 2003144307	A1	20030731	US 2002-315633	20021210
	US 6753427	B2	20040622		
PRAI	US 2000-229584P	P	20000831		
	US 2000-229577P	P	20000831		
	WO 2001-EP9689	W	20010822		
	US 2001-943338	A3	20010830		
	US 2001-943407	A1	20010830		
OS	MARPAT 136:232316				
GI					



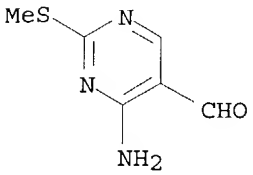
AB Compds. I are disclosed [wherein: R1 = H or alkyl; R2 = substituted cycloalkyl, hetero-substituted cycloalkyl, heteroalkyl-substituted cycloalkyl, hetero-substituted cycloalkyl-aryl, heterocyclyl, heterocyclylspirocycloalkyl, aralkoxy, alkoxy, -alkylene-S(O)n-alkyl (where n = 1 or 2) or SO2Ar2; R3 = H, amino, monoalkylamino, dialkylamino, acylamino, NRaC(:O)Rb (where Ra = H or alkyl, and Rb = heterocyclyl or heteroalkyl), alkyl, cycloalkyl, aryl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, -alkylene-C(O)R (where R = H, alkyl, OH, alkoxy, amino, monoalkylamino or dialkylamino), acyl, or phthalimidoalkyl; and each of Ar1 and Ar2 = aryl]. Also disclosed in claims is their use for treatment of disorders selected from the group consisting of arthritis, Crohn's disease, Alzheimer's disease, irritable bowel syndrome, adult respiratory distress syndrome, and chronic obstructive pulmonary disease. A list of 151 compds. I is given, as well as approx. 100 synthetic examples. For instance, cyclocondensation of 4-amino-2-(methylthio)pyrimidine-5-carboxaldehyde with Et (2-chlorophenyl)acetate, followed by oxidation of the sulfide to a sulfone with Oxone, and displacement of the Me sulfone with trans-4-aminocyclohexanol, gave 78% title compound II. In an in vitro p38

assay, I had IC50 values ranging from about 4.76 .mu.M to about 0.0003 .mu.M.

IT **770-31-0P**, 4-Amino-2-(methylthio)pyrimidine-5-carboxaldehyde
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of oxopyridopyrimidines as p38 kinase inhibitors)

RN 770-31-0 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



IT **770-31-0P**, 4-Amino-2-(methylthio)pyrimidine-5-carboxaldehyde **185040-32-8P**, 4-(Methylamino)-2-(methylthio)pyrimidine-5-carboxaldehyde **211247-46-0P**, 4-(Cyclopropylamino)-5-formyl-2-(methylthio)pyrimidine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of oxopyridopyrimidines as p38 kinase inhibitors)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:171895 HCAPLUS

DN 136:216763

TI Preparation of 7-oxopyridopyrimidines as p38 MAP kinase inhibitors

IN Arzeno, Humberto Bartolome; Chen, Jian Jeffrey; Dunn, James Patrick; **Goldstein, David Michael**; **Lim, Julie Anne**

PA F. Hoffmann-La Roche Ag, Switz.

SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2

DT Patent

LA English

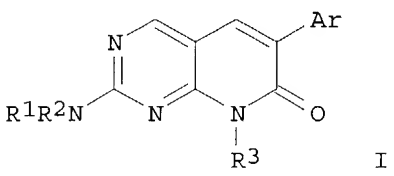
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002018379	A2	20020307	WO 2001-EP9688	20010822
	WO 2002018379	A3	20020725		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002012147	A5	20020313	AU 2002-12147	20010822
	EP 1315727	A2	20030604	EP 2001-980258	20010822
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001013590	A	20030722	BR 2001-13590	20010822
	JP 2004507540	T2	20040311	JP 2002-523894	20010822

	US 2002055513	A1	20020509	US 2001-943338	20010830
	US 6518276	B2	20030211		
	US 2003153586	A1	20030814	US 2002-230723	20020829
	US 2003144307	A1	20030731	US 2002-315633	20021210
	US 6753427	B2	20040622		
PRAI	US 2000-229577P	P	20000831		
	US 2000-229584P	P	20000831		
	WO 2001-EP9688	W	20010822		
	US 2001-943338	A3	20010830		
	US 2001-943407	A1	20010830		

OS MARPAT 136:216763

GI



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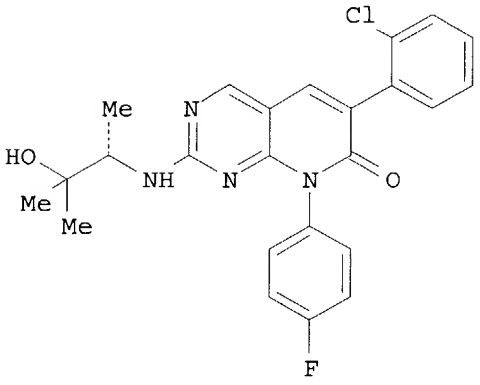


II

AB The present invention provides compds. of the formula I [R1 = H, alkyl; R2 = alkoxy-substituted alkyl, heterocyclyl, cycloalkyl; etc.; R1R2 = heterocyclyl; R3 = H, alkyl, amino, aryl, acyl, etc.; Ar = aryl], a prodrug or a pharmaceutically acceptable salt thereof, and processes for their preparation and their use for the treatment of p38 mediated disorders. Thus, II was prepared and inhibited p38 MAP kinase in vitro with IC50 of 0.0003 .mu.M.

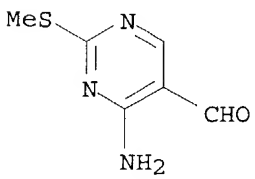
IT **770-31-0P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 7-oxopyridopyrimidines as p38 MAP kinase inhibitors)

RN 770-31-0 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



IT **770-31-0P 185040-32-8P**

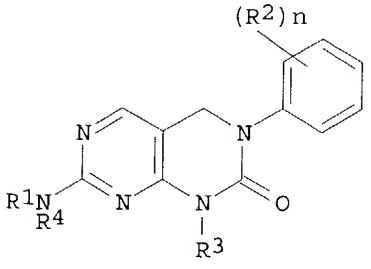
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 7-oxopyridopyrimidines as p38 MAP kinase inhibitors)

L33 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:300721 HCAPLUS
DN 134:326540
TI Preparation of alkylamino substituted bicyclic nitrogen heterocycles for pharmaceutical use as inhibitors of p38 protein kinase
IN Dunn, James Patrick; Fisher, Lawrence Emerson; **Goldstein, David Michael**; Harris, William; Hill, Christopher Huw; Smith, Ian Edward David; Welch, Teresa Rosanne
PA F. Hoffmann-La Roche Ag, Switz.
SO PCT Int. Appl., 177 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001029042	A1	20010426	WO 2000-EP10088	20001013
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 2000015243	A	20020716	BR 2000-15243	20001013
	EP 1228070	A1	20020807	EP 2000-967864	20001013
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	TR 200201057	T2	20020923	TR 2002-200201057	20001013
	JP 2003512378	T2	20030402	JP 2001-531840	20001013
	NZ 518119	A	20040227	NZ 2000-518119	20001013
	US 6451804	B1	20020917	US 2000-693337	20001020
	ZA 2002002540	A	20030630	ZA 2002-2540	20020328
	NO 2002001781	A	20020418	NO 2002-1781	20020416
PRAI	US 1999-160803P	P	19991021		
	US 2000-213743P	P	20000622		
	WO 2000-EP10088	W	20001013		

OS MARPAT 134:326540
GI



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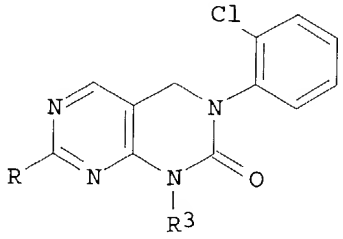


II

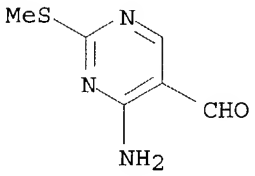
AB Alkylamino-substituted dihydropyrimido[4,5-d]pyrimidinone derivs., such as I [R1 = H, alkyl, alkenyl, alkynyl, acyl, cycloalkyl, etc.; R2 = vinyl,

alkyl, halogen, heteroalkyl; R3 = alkyl, heteroalkyl, cycloalkyl, heterocyclyl, etc.; R4 = H, alkyl, etc.; n = 0-3], were prepared for pharmaceutical use. The compds. are p38 inhibitors and may be used in the treatment of arthritis, Crohn's disease, irritable bowel syndrome, adult respiratory distress syndrome, chronic obstructive pulmonary disease, osteoporosis, or Alzheimer's disease. Thus, dihydropyrimido[4,5-d]pyrimidinone II (R = NHCMe2CH2OH, R3 = Me) was prepared via a substitution reaction of H2NCMe2CH2OH with sulfone II (R = SO2Me, R3 = Me) when combined and heated to 100-110.degree. for 1 h. The prepared dihydropyrimido[4,5-d]pyrimidinone derivs. showed 50% p38 inhibitory activity at concns. < 10 .mu.M.

IT **770-31-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of alkylamino substituted pyrimidino[4,5-d]pyrimidines for pharmaceutical use as inhibitors of p38 protein kinase)

RN 770-31-0 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



IT **770-31-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of alkylamino substituted pyrimidino[4,5-d]pyrimidines for pharmaceutical use as inhibitors of p38 protein kinase)

IT **185040-32-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of alkylamino substituted pyrimidino[4,5-d]pyrimidines for pharmaceutical use as inhibitors of p38 protein kinase)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d bib abs hitstr l44 tot

L44 ANSWER 1 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:412945 HCAPLUS
DN 140:423693
TI Preparation of pyrimido Src tyrosine kinase inhibitors as anti-proliferative agents for the treatment of cancer
IN Luk, Kin-Chun; Rossman, Pamela Loreen; Scheiblich, Stefan; So, Sung-Sau
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004041821	A1	20040521	WO 2003-EP11892	20031027 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,

GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG

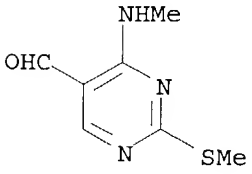
US 2004110773 A1 20040610 US 2003-689438 20031020 <--
PRAI US 2002-423670P P 20021104 <--
OS MARPAT 140:423693
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB MovPyrimido compds. I (R1 = H, alkyl, substituted alkyl, aryl, heteroaryl, heterocycle, cycloalkyl, alkenyl, alkynyl; R2,R3,R4 independently = H, amine, alkoxy, sulfanyl, alkyl, cycloalkyl, alkenyl, alkynyl; R5, R6, R7, R8 independently = H, lower alkyl, amine, OH, alkoxy, sulfanyl, halogen, ketone, ester, amide, sulfonyl, CN; R9 = H, diester, ketone), that are selective inhibitors of the Src family of tyrosine kinases are prepared for the treatment of breast, colon, pancreatic, and hepatic cancers. Thus, 1-(2,4-dichloro-pyrimidin-5-yl)-ethanol was treated with phosphorus oxybromide and diisopropyl amine to give 2,4-dichloro-5-(1-bromoethyl)-pyrimidine which was treated with p-anisidine, potassium carbonate, and potassium iodide to give the corresponding amine. The above amine was reacted with 3-cyanophenyl isocyanate in toluene to give II. II was reacted with acetic acid 2-(3-amino-phenyl)-Et ester, followed by treatment with potassium carbonate in methanol to give III. III showed and IC50 of less than 1.0 .mu.M against Src tyrosine kinase. Also disclosed are pharmaceutical compns. containing these compds. and the use for treating cancer.

IT **185040-32-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrimido Src tyrosine kinase inhibitors as anti-proliferative agents for the treatment of cancer)

RN 185040-32-8 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



L44 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:372873 HCAPLUS
DN 140:391294
TI Preparation of amino-substituted dihydropyrimido[4,5-d]pyrimidinone derivatives as inhibitors of src family tyrosine kinases
IN Cai, Jianping; Dimoudis, Nikolaos; Honold, Konrad; Luk, Kin-Chun;

Scheiblich, Stefan; Sudergat, Hilke; Tiefenthaler, Georg; Tonn, Oliver

PA USA

SO U.S. Pat. Appl. Publ., 31 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004087600	A1	20040506	US 2003-697543	20031030 <--
	WO 2004041823	A1	20040521	WO 2003-EP12203	20031103 <--

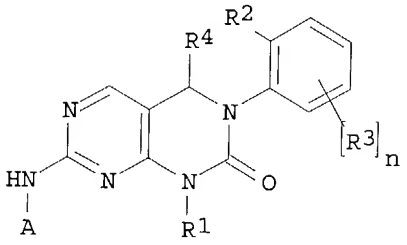
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2002-24573 A 20021104 <--

OS MARPAT 140:391294

GI



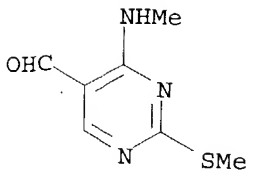
I

AB The title compds. [I; R1 = H, alkyl, aryl, etc.; R2 = halo, CN, CF3; R3 = halo, OH, CN, etc.; n = 0-2; R4 = H, alkyl, alkoxy, CN; A = (un)substituted 2,3-dihydrobenzo[1,4]dioxin-6-yl, benzodioxane-6-yl, 3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-7-yl, etc.] which are protein kinase inhibitors, in particular they inhibit the src family tyrosine kinases, and therefore useful for the treatment of diseases mediated by src tyrosine kinases, including cell proliferative disorders such as cancer, were prepared Thus, reacting 3-(2-bromophenyl)-3,4-dihydro-7-methanesulfonyl-1-methylpyrimido[4,5-d]pyrimidin-2(1H)-one with 2-hydroxymethyl-6-amino-1,4-benzodioxane (preparation given) afforded 3-(2-bromophenyl)-7-(2-hydroxymethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2(1H)-one which showed IC50 of 7.5 nM against src kinase, and IC50 of 6.3 nM against lck kinase. The pharmaceutical composition containing the compound I is claimed.

IT **185040-32-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino-substituted dihydropyrimido[4,5-d]pyrimidinones as inhibitors of src family tyrosine kinases)

RN 185040-32-8 HCAPLUS

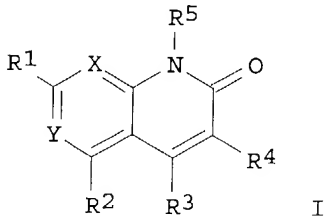
CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



L44 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:218763 HCAPLUS
DN 140:247112
TI Pharmaceutical compositions containing pyridopyrimidines or naphthyridines as phosphodiesterase V inhibitors with fewer adverse effects
IN Yamada, Koichiro; Hikota, Masatake; Koga, Yuichi; Yoshikawa, Kohei; Omori, Kenji
PA Tanabe Seiyaku Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 57 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2004083587	A2	20040318	JP 2003-287628	20030806 <--
PRAI JP 2002-228526	A	20020806 <--		

OS MARPAT 140:247112
GI

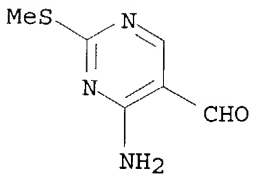


I

AB Title compns., useful for prophylactic and therapeutic treatment of impotence, pulmonary hypertension, diabetic gastroparesis, female sexual dysfunction, heart failure, prostatomegaly, and prospermia, contain I [R1 = (un)substituted N-containing heterocyclyl, (un)substituted amino, (un)substituted lower alkoxy; R2 = H, lower alkyl; R3 = H, (un)substituted lower alkyl, (un)substituted heteroaryl; R4 = H, lower alkyl, (esterified or amidated) carboxyl; R5 = (un)substituted lower alkyl; X, Y = C, N; X = Y .noteq. C] or their pharmacol. acceptable salts as active ingredients. Thus, (S)-I (R1 = 2-hydroxymethyl-1-pyrrolidinyl, R2-R4 = H, R5 = 3-chloro-4-methoxybenzyl, X = Y = N) inhibited dog PDE V with IC50 of 3.26 nM.

IT **770-31-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyridopyrimidines or naphthyridines as phosphodiesterase V inhibitors for treatment of diseases)
RN 770-31-0 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

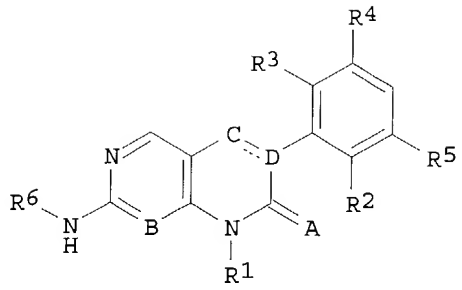


L44 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:80385 HCAPLUS
DN 140:146153
TI Preparation of pyrimidopyrimidinones as kinase inhibitors
IN Chivikas, Connolly Cleo J.; Deur, Christopher James; Hamby, James Marino; Hoyer, Denton Wade; Limberakis, Chris; Reed, Jessica Elizabeth; Schroeder, Mel Conrad; Taylor, Clarke
PA USA
SO U.S. Pat. Appl. Publ., 44 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

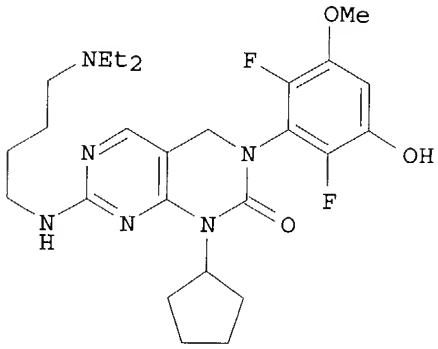
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004019210	A1	20040129	US 2003-621983	20030717 <--
WO 2004011465	A1	20040205	WO 2003-IB3359	20030721 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-398638P P 20020725 <--
OS MARPAT 140:146153
GI



I



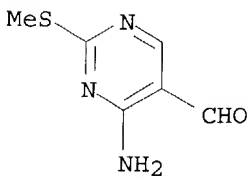
II

AB This invention provides phenyl-substituted pyrimidopyrimidines, dihydropyrimidopyrimidines, pyridopyrimidines, naphthyridines, and pyridopyrazines of the general formula I [A = O, NH2, mono(or di)alkylamino, NHCONHR12 (wherein R12 = alkyl, alkylenecycloalkyl); B, C, D = CH, N (with the proviso that C and D are not both N); R1 = alkyl (optionally substituted by CO2H), (un)substituted Ph, CH2Ph, piperidinyl, etc.; R2 = H, Cl, F; R3 = H, Cl, F (at least one of R2 or R3 = F); R4 = H, OH, OMe, OEt (if R4 = H, R2 and R3 is not H); R5 = OMe, OEt; R6 = H, alkyl-NH2, O-alkyl-NH2, etc.] that inhibit cyclin-dependent kinase and tyrosine kinase enzymes, methods and intermediates for their synthesis, as well as pharmaceutical compns. and methods for their use in treating, inhibiting or preventing maladies associated with cell proliferative disorders, including angiogenesis, atherosclerosis, restenosis, and cancer (no biol. data given). Synthesis of 35 title compds. I is described. E.g., a multi-step synthesis of II was given.

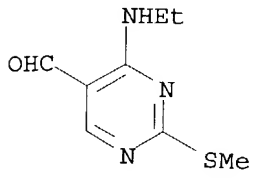
IT **770-31-0 185040-35-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrimidopyrimidinones as kinase inhibitors)

RN 770-31-0 HCAPLUS

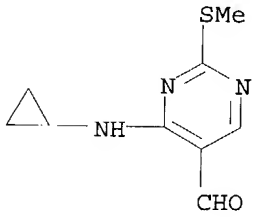
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 185040-35-1 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



IT **211247-46-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrimidopyrimidinones as kinase inhibitors)
RN 211247-46-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(cyclopropylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



L44 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:719487 HCAPLUS
DN 139:246044
TI Bicyclic pyridine and pyrimidine derivatives, e.g., thieno[2,3-d]pyrimidines and analogs, active as p38 kinase inhibitors, and their preparation, pharmaceutical compositions, and uses
IN Chen, Jian Jeffrey; Dewdney, Nolan James; Stahl, Christoph Martin
PA F. Hoffman-La Roche Ag, Switz.
SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003074530	A1	20030912	WO 2003-EP2090	20030228 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2003207900	A1	20031106	US 2003-383392	20030306 <--
PRAI	US 2002-362373P	P	20020307 <--		
	US 2002-430508P	P	20021203 <--		
OS	MARPAT 139:246044				
GI					

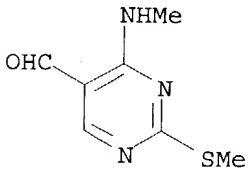
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention discloses compds. I, their pharmaceutical formulations, methods of making them, and their uses in the treatment of p38 kinase-mediated diseases [wherein: A is N or CH; R1 is H, alkyl or arylalkyl; R2 is alkyl, hydroxyalkyl, (R'')2NCO-alkylene- (where each R'' is independently H or alkyl), cycloalkyl, heterocyclyl, aryl, heteroaryl, or heteroalkyl; X is O, NR3, or S, wherein R3 is H, alkyl, or aryl; and Y is bond, O, NR', CO, CH(OR'), CH(R'), or S(O)n, wherein n = 0-2; and R' is H or alkyl; and R is aryl or heteroaryl; or an isomer, a pharmaceutically acceptable salt, an ester, or a prodrug thereof]. The compds. are useful for treatment of disorders exacerbated or caused by excessive or unregulated TNF or p38 kinase production Claimed methods of treatment include uses for treatment of arthritis, Crohn's disease, Alzheimer's disease, irritable bowel syndrome, adult respiratory distress syndrome, and chronic obstructive pulmonary disease. A table of over 40 compds. I is given, and most of these compds. are also claimed individually. The example compds. are mostly thienopyrimidines, but include some furanopyrimidines and pyrrolopyrimidines. For instance, invention compound II (as the HCl salt) was prepared from 4-chloro-2-(methylthio)pyrimidine in 5 steps: (1) fluorination of chloro using KF and 18-crown-6 in tetraglyme; (2) lithiation in the 5-position with LDA and formylation with EtOCHO; (3) cyclocondensation of the resultant aldehyde with 2'-ClC6H4COCH2SH to form a fused thiophene ring; (4) oxidation of the methylthio group to a Me sulfone using Oxone; and (5) aminolysis of the sulfone with 4-aminotetrahydropyran, followed by chromatog. and acidification in ether. In a test for inhibition of recombinant p38 kinase in vitro, invention compound III gave an IC50 of 104 nM.

IT **185040-32-8P**, 4-(Methylamino)-2-(methylthio)pyrimidine-5-carboxaldehyde
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of thienopyrimidines and analogs as p38 kinase inhibitors)

RN 185040-32-8 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:261843 HCAPLUS
DN 138:287695
TI Process for preparing 2-[(4-pyridyl)amino]-6-(dialkyloxyphenyl)pyrido[2,3-d]pyrimidin-7-ones, useful as anticancer agents, by amination of 2-(alkylsulfanyl)pyrido[2,3-d]pyrimidine derivatives with 4-aminopyridines
IN Tjiong, Howard Isaac; Winters, Roy Thomas
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003027110	A2	20030403	WO 2001-US51422	20010712 <--
	WO 2003027110	A3	20040226		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 2001013037	A	20040120	BR 2001-13037	20010712 <--
	EP 1417207	A2	20040512	EP 2001-274395	20010712 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003176700	A1	20030918	US 2003-343803	20030204 <--
PRAI	US 2000-222866P	P	20000804 <--		
	WO 2001-US51422	W	20010712 <--		

OS CASREACT 138:287695; MARPAT 138:287695
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

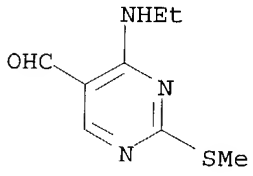
AB A one-step process for preparing 2-(pyridylamino)pyrido[2,3-d]pyrimidines I is disclosed [wherein Ar is aryl, R' and R'' are H, alkyl, halogen, or Ph, and R2 is (especially) alkyl, H, (un)substituted (CH2)0-3Ph, heteroaryl, cycloalkyl, etc.]. The process involves reaction of a 4-aminopyridine II with an alkali metal amide or hydride, and with a 2-(alkylsulfanyl)pyrido[2,3-d]pyrimidine derivative III. I are obtained in high yield and excellent purity. Prior art methods involve oxidation of sulfides III to sulfoxides, and displacement of sulfinate from these with II. The new method, which displaces alkylthiolates from III directly without the need for oxidation, avoids the dangers, expenses, added reactions, over-oxidns., and/or extra isolations which would accompany an industrial-scale oxidation step. Compds. I are known inhibitors of protein tyrosine kinase, with antiangiogenic activity, and are useful for treatment of cancer (no data). For example, Et 4-chloro-2-(methylthio)-5-pyrimidinecarboxylate reacted with EtNH2 and Et3N in THF to give 95% of its 4-ethylamino analog, which underwent LiAlH4 reduction of the ester to an alc., and reoxidn. of this with MnO2 (90%), to give 4-(ethylamino)-2-(methylsulfanyl)pyrimidine-5-carboxaldehyde. This ortho-amino aldehyde was cyclocondensed with 3,5-(MeO)2C6H3CH2CO2Et in DMSO in the presence of DBU at 45-50.degree. to give 84% III [Ar = 3,5-(MeO)2C6H3, Alkyl = Me, R2

= Et]. Reaction of the latter with 4-aminopyridine and LiNH2 in THF at 50.degree. gave 93.6% yield of title compound IV with purity 98.5% by HPLC.

IT **185040-35-1P**, 4-(Ethylamino)-2-(methylsulfanyl)pyrimidine-5-carboxaldehyde
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (pyridylamino)pyridopyrimidinone anticancer agents by amination of (alkylsulfanyl)pyridopyrimidinone derivs. with aminopyridines)

RN 185040-35-1 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)

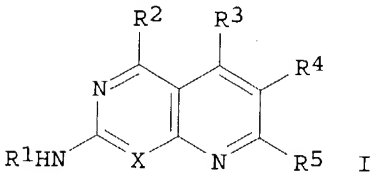


L44 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:868935 HCAPLUS
DN 137:370104
TI Preparation of pyridopyrimidinamines as kinase inhibitors for the treatment of hyperproliferative diseases
IN Parrish, Cynthia A.; Lago, Maria Amparo; Semones, Marcus A.
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002090360	A1	20021114	WO 2002-US15176	20020510 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-289951P P 20010510 <--
OS MARPAT 137:370104
GI



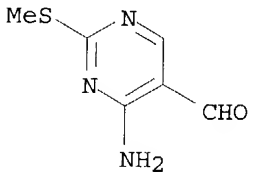
I

AB Title compds. [I; X = N, CR3; R1 = alkyl, alkanoyl, alkenyl, alkynyl, cycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, etc.; R2 = H, alkyl, alkanoyl, alkenyl, alkynyl, cycloalkyl, alkylaryl, alkylheterocyclyl, CF3, halo, SO2CF3, etc.; R3 = H, alkyl, alkanoyl, alkenyl, alkynyl, cycloalkyl, alkylaryl, alkylheteroaryl, cyano, CF3, SCF3, SOCF3, SO2CF3, etc.; R4 = alkyl, alkanoyl, alkenyl, alkynyl, cycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, cyano, CF3, SCF3, SOCF3, SO2CF3, halo, etc.; R5 = alkyl, alkanoyl, alkenyl, alkynyl, cycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, cyano, CF3, etc.; all groups may be substituted], were prepared for treatment of cancer and benign proliferative diseases (no data). Thus, crude 2-methanesulfinyl-6,7-diphenylpyrido[2,3-d]pyrimidine and 4-(2-diethylaminoethoxy)aniline were refluxed 14 h in PhMe to give [4-(2-diethylaminoethoxy)phenyl]-(6,7-diphenylpyrido[2,3-d]pyrimidin-2-yl)amine.

IT **770-31-0**, 4-Amino-2-methylthiopyrimidine-5-carboxaldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyridopyrimidinamines as kinase inhibitors for treatment of hyperproliferative diseases)

RN 770-31-0 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



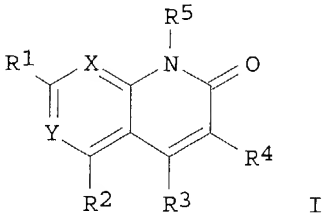
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:676017 HCAPLUS
DN 137:201330
TI Preparation of pyridopyrimidine or naphthyridine derivatives as PDE V inhibitors
IN Yamada, Koichiro; Hikota, Masataka; Koga, Yuichi; Kikkawa, Kohei; Omori, Kenji
PA Tanabe Seiyaku Co., Ltd., Japan
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002068419	A1	20020906	WO 2002-JP1638	20020225 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
JP 2002322179 A2 20021108 JP 2002-47528 20020225 <--
EP 1364950 A1 20031126 EP 2002-700731 20020225 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
NZ 527741 A 20031219 NZ 2002-527741 20020225 <--
PRAI JP 2001-49879 A 20010226 <--
WO 2002-JP1638 W 20020225 <--
OS MARPAT 137:201330
GI

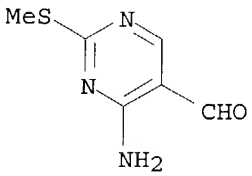


I

AB The title compds. I [R1 is optionally substituted nitrogenous heterocyclic group, etc.; R2 is hydrogen or lower alkyl; R3 is hydrogen, optionally substituted lower alkyl, etc.; R4 is hydrogen, lower alkyl, COOH, etc.; R5 is hydrogen, optionally substituted aryl, etc.; and one of X and Y is CH and the other is nitrogen, or both of X and Y are nitrogen] are prepared I are said to have excellent PDE V inhibitory activity (no data) and are useful as a preventive/remedy for erectile dysfunction.

IT **770-31-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyridopyrimidine or naphthyridine derivs. as PDE V inhibitors)

RN 770-31-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:123003 HCAPLUS
DN 136:183833
TI Preparation of 2-(4-pyridyl)amino-6-dialkoxyphenyl-pyrido[2,3-d]pyrimidin-7-ones as novel antiangiogenic agents useful for the treatment of diseases associated with aberrant blood vessel proliferation.
IN Hamby, James Marino; Klutchko, Sylvester; Kramer, James Bernard
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 51 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002012238	A2	20020214	WO 2001-US22881	20010720 <--
	WO 2002012238	A3	20020510		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001077032	A5	20020218	AU 2001-77032	20010720 <--
	EP 1307450	A2	20030507	EP 2001-954811	20010720 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004519422	T2	20040702	JP 2002-518213	20010720 <--
	US 2003220345	A1	20031127	US 2003-343847	20030204 <--
PRAI	US 2000-223083P	P	20000804 <--		
	WO 2001-US22881	W	20010720 <--		

OS MARPAT 136:183833
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

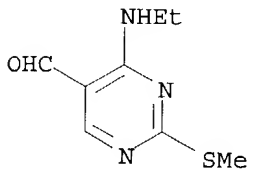
AB The invention discloses the preparation and the use of title compds. I, wherein: R1, R2, R5, R6 = H, halogen, alkyl, alkoxy, thio, thioalkyl, hydroxy, alkanoyl, nitrile, nitro, alkanoyloxy, CF3, alkyl ester, NH2 or derivs., aminoalkoxy, etc.; R3, R4 = alkyl, or haloalkyl; R7 = H, alkyl, alkenyl, alkynyl, or cycloalkyl; including their pharmaceutically acceptable salts and compns. as antiangiogenic agents. Compds. I, are useful for treating diseases, resulting from uncontrolled cellular proliferation such as cancer, atherosclerosis, rheumatoid arthritis, and psoriasis. The invention compds. exhibited greater selectivity for inhibiting VEGF and FGF, without inhibiting the Src family c-Src and Lck kinases. Claims include 12 specific compds. and the syntheses of 5 especially preferred compds. are described. For example, condensation of 3,5-dimethoxyphenylacetonitrile with aldehyde II, followed by acylation of the resultant imine, hydrolysis, oxidation, and sulfoxide displacement with the lithium salt of 4-amino-2,6-dimethoxypyridine, provided the most preferred compound III in 5 steps. Tyrosine kinase inhibition data (IC50 = .mu.M) was disclosed for compound I (R1, R5, R6 = H; R2 = 3-Cl; R3, R4 = Me; and R7 = Et) against: FGFr = 0.0002, VEGF-2 = 0.003, PDGF = 5, Lck = 2.77, and c-Src = >4. Inhibition of serum-stimulated HUVEC cell proliferation data (IC50 = .mu.M) of compound I (R1, R2, R5, R6 = H; R3, R4 = Me; and R7 = Et) against HUVEC = 0.009, A90 = 2.92, and C6 = >25 uM was also provided. Metabolic stability and transport studies of compound I (R1, R2, R5, R6 = H; R3, R4 = Me; and R7 = Et) with human and mice liver S9 prepns. indicated half-lives > 200 min. Also investigated, the in vivo anticancer efficacy of compound I (R1, R2, R5, R6 = H; R3, R4 = Me; and R7 = Et) against mammary adenocarcinoma M16/C: at 5 mg/kg dosage yielded a median mass of treated tumors/median mass of control tumor ratio of 39% with a net gain in

subject body weight

IT **185040-35-1P**, 4-Ethylamino-2-methylsulfanylpyrimidine-5-carboxaldehyde
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrido[2,3-d]pyrimidine-7-ones as antiangiogenic agents)

RN 185040-35-1 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



L44 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:123002 HCAPLUS

DN 136:167386

TI Preparation of 2-(4-pyridyl)amino-6-dialkyloxyphenyl-pyrido[2,3-d]pyrimidin-7-ones

IN Beylin, Vladimir Genukh; Lee, Richard Jungkyu; Marlatt, Mark Eugene

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2

DT Patent

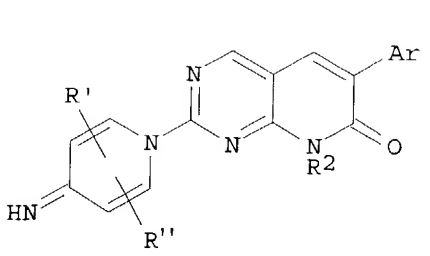
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002012237	A2	20020214	WO 2001-US22001	20010712 <--
	WO 2002012237	A3	20020510		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001078908	A5	20020218	AU 2001-78908	20010712 <--
	EP 1307451	A2	20030507	EP 2001-957137	20010712 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001012861	A	20030701	BR 2001-12861	20010712 <--
	JP 2004505974	T2	20040226	JP 2002-518212	20010712 <--
	US 2003216415	A1	20031120	US 2003-343805	20030204 <--
PRAI	US 2000-223084P	P	20000804 <--		
	WO 2001-US22001	W	20010712 <--		

OS MARPAT 136:167386

GI



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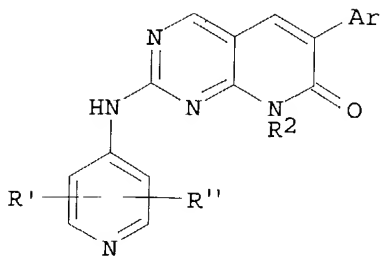

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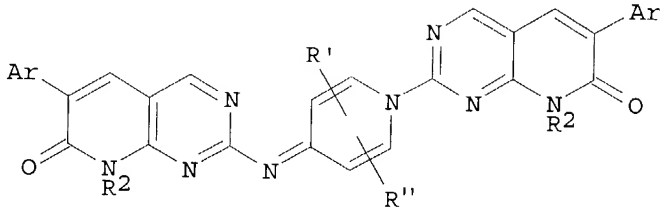


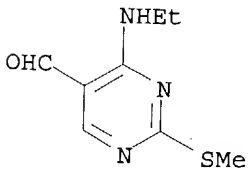
III

AB 2-Pyridylaminopyrido[2,3-d]pyrimidines with formula I are prepared by the reaction of a 4-aminopyridine compound with 2-(4-imino-4H-pyridin-1-yl)pyrido[2,3-d]pyrimidine II (Ar = aryl; R', R'' = H, alkyl, alkoxy, Ph; R2 = alkyl). Preparation of intermediate 2-alkylsulfanylpyridopyrimidine III by the reaction of an arylacetic acid ester with a 2-alkylsulfanyl-4-alkylaminopyrimidine-5-carboaldehyde is also claimed.

IT **185040-35-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-(4-pyridyl)amino-6-dialkyloxyphenylpyrido[2,3-d]pyrimidin-7-ones)

RN 185040-35-1 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



L44 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:565041 HCAPLUS

DN 135:152818

TI Preparation of 2-amino-8H-pyrido[2,3-d]pyrimidin-7-ones as cyclin dependent kinase inhibitors for treatment of neurodegenerative disease

IN Booth, Richard John; Chatterjee, Arindam; Malone, Thomas Charles

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 232 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 2001055148	A1	20010802	WO 2000-US32572	20001130 <--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 2000017075	A	20021105	BR 2000-17075	20001130 <--
	EP 1255755	A1	20021113	EP 2000-980883	20001130 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003523358	T2	20030805	JP 2001-561007	20001130 <--
PRAI	US 2000-178400P	P	20000127 <--		
	WO 2000-US32572	W	20001130 <--		

OS MARPAT 135:152818

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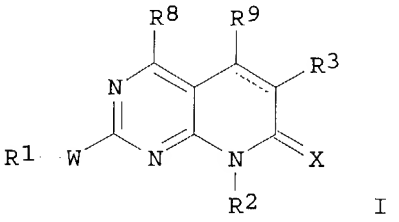

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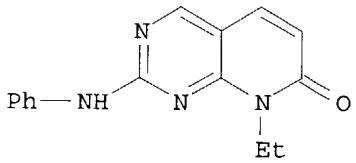


II

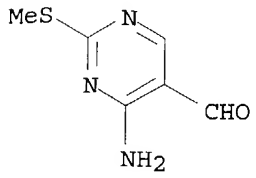
AB This invention provides a method for treating neurodegenerative diseases in mammals comprising administering an effective amount of a cyclin-dependent kinase (cdk) inhibitor (I) [wherein W = NH, S, SO, or SO2; X = O or NH; R1 and R2 = independently H or (un)substituted (CH2)nAr, (CH2)nheteroaryl, (CH2)nheterocyclyl, (cyclo)alkyl, alkenyl, or alkynyl; R3 = H or alkyl; R4 and R5 = independently H, (un)substituted alkyl, alkenyl, alkynyl, (CH2)nAr, cycloalkyl, heterocyclyl, or heteroaryl; or R4 and R5 together with the N to which they are attached may form a heterocycle; R6 = alkyl; R8 and R9 = independently H, (thio)alkyl, NR4R5, N(O)R4R5, NR4R5R6Y, OH, alkoxy, SH, halo, COR4, CO2R4, CONR4R5, SO2NR4R5, SO3R4, PO3R4, CHO, CN, nor NO2; Y = halo counterion; n = 0-3]. Examples include prepns. and/or enzyme assay data for over 600 invention compds. For instance, 4-ethylamino-2-phenylaminopyrimidine-5-carboxaldehyde (multi-step preparation given) was heated with (carbethoxymethylene)triphenylphosphorane at reflux to give the acrylate (86%), which was cyclized using 1,8-diazabicyclo[5.4.0]undec-7-ene in TEA to afford II. The latter inhibited cdk4/D, cdk2/E, cdk2/A, cdk1/B, and cdk5 with IC50 values of 0.752 .mu.M, 0.41 .mu.M, 0.129 .mu.M, 1.015 .mu.M, and 0.065 .mu.M, resp. Due to their relative selectivity for inhibition of cdk5 over other cdk enzymes, I are particularly useful for the treatment of neurodegenerative diseases.

IT **770-31-0P 185040-32-8P 185040-35-1P 211247-46-0P**

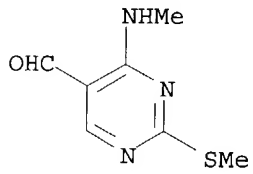
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of 2-amino-8H-pyrido[2,3-d]pyrimidinones as cyclin-dependent kinase inhibitors by cyclization of 3-[2-(methylsulfinyl)-4-aminopyrimidin-5-yl]acrylates or acrylonitriles)

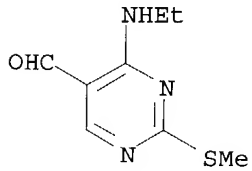
RN 770-31-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



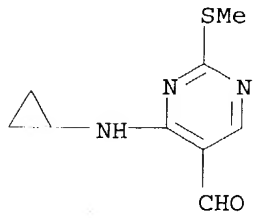
RN 185040-32-8 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RN 185040-35-1 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RN 211247-46-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(cyclopropylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:565040 HCAPLUS
DN 135:152817

TI Preparation of pyrido[2,3-d]pyrimidine-2,7-diamine kinase inhibitors for treatment of proliferative disorders

IN Booth, Richard John; Dobrusin, Ellen Myra; Josyula, Vara Prasad Venkata Nagendra; McNamara, Dennis Joseph; Toogood, Peter Laurence

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 114 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001055147	A1	20010802	WO 2001-IB69	20010123 <--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1254137	A1	20021106	EP 2001-900591	20010123 <--
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	BR 2001007751	A	20021112	BR 2001-7751	20010123 <--
	JP 2003523357	T2	20030805	JP 2001-561006	20010123 <--
	EE 200200405	A	20031215	EE 2002-405	20010123 <--
	BG 106850	A	20030228	BG 2002-106850	20020620 <--
	NO 2002003527	A	20020910	NO 2002-3527	20020724 <--
	US 2003073668	A1	20030417	US 2002-182178	20020724 <--
PRAI	US 2000-178261P	P	20000125 <--		
	WO 2001-IB69	W	20010123 <--		

OS MARPAT 135:152817

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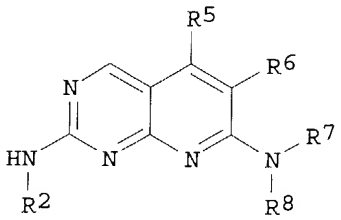

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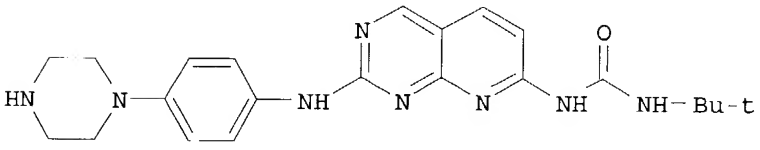


II

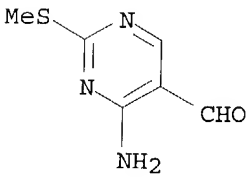
AB Title compds. (I) [wherein R2, R7, R13, R14, and R15 = independently H, or (un)substituted alkyl, alkenyl, alkynyl, or (CH2)nR12; R5 = halo, CN, NO2, R9, NR9R10, or OR9; R6 = halo, CN, NO2, R9, NR9R10, OR9, CO2R9, COR9,

CONR9R10, NR9COR10, or (un)substituted alkenyl or alkynyl; R8 = CO2R13, COR13, CONR13R14, CSNR13R14, C(NR13)NR14R15, SO3R13, SO2R13, SO2NR13R14, PO3R13R14, POR13R14, or PO(NR13R14)2; R9 and R10 = independently H or (un)substituted alkyl; R11 = heteroaryl or heterocyclic group; R12 = cycloalkyl, heterocyclic, or (hetero)aryl group; n = 0-3; and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof] were prepared and formulated as cyclin dependent kinase (cdk) and growth factor-mediated tyrosine kinase inhibitors. For example, the 2-methylsulfinyl group of 2-methanesulfinylpyrido[2,3-d]pyrimidin-7-ylamine was displaced by 4-(4-aminophenyl)piperazine-1-carboxylic acid tert-Bu ester (multi-step preparation of starting materials given) by refluxing in DMSO (36%). The pyrido[2,3-d]pyrimidin-7-amine was converted to the urea by reaction with tert-Bu isocyanate (67.9%) and the piperazine deprotected using HCl/dioxane (93.4%) to afford II.bul.2.1HCl. The latter inhibited the cyclin dependent kinases cdk1/B, cdk2/A, cdk2/E, and cdk4D with IC50 values of 0.219 .mu.M, 0.060 .mu.M, 0.130 .mu.M, and 0.006 .mu.M, resp. In addition, II.bul.2.1HCl inhibited the growth factor receptor tyrosine kinases PDGF-.beta. and FGF-1 by 94.4% and 93.7%, resp., at 50 .mu.M. I are useful for treating cell proliferative disorders, such as cancer and restenosis (no data).

IT **770-31-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrido[2,3-d]pyrimidine-2,7-diamines kinase inhibitors by cyclization of 3-[2-(methylsulfinyl)-4-aminopyrimidin-5-yl]acrylates or [2,4-diaminopyrimidine-5-yl]ketones)

RN 770-31-0 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



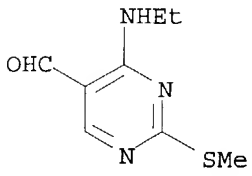
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:108404 HCAPLUS
DN 137:181455
TI Pyrido[2,3-d]pyrimidin-7-one Inhibitors of Cyclin-Dependent Kinases. [Erratum to document cited in CA134:127686]
AU Barvian, Mark; Boschelli, Diane H.; Cossrow, Jennifer; Dobrusin, Ellen; Fattaey, Ali; Fritsch, Alex; Fry, David; Harvey, Patricia; Keller, Paul; Garrett, Michelle; La, Frances; Leopold, Wilbur; McNamara, Dennis; Quin, Maire; Trumpp-Kallmeyer, Susanne; Toogood, Peter; Wu, Zhipei; Zhang, Erli
CS Departments of Chemistry and Cancer Research, Parke-Davis Pharmaceutical Research Division, Warner Lambert Company, Ann Arbor, MI, 48105, USA
SO Journal of Medicinal Chemistry (**2001**), 44(6), 1016
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB On page 4607, in the legend to Scheme 1, Ph3PC=CO2Et should be written as Ph3P=CHCO2Et. On page 4609, in Table 3, the IC50 value for compound 58

should be recorded as 0.007 .mu.M, not 0.0007 .mu.M.

IT **185040-35-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and structure-activity relationships of pyridopyrimidinone as inhibitors of cyclin-dependent kinases (Erratum))

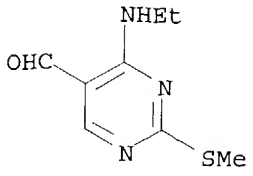
RN 185040-35-1 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



L44 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:792832 HCAPLUS
DN 134:127686
TI Pyrido[2,3-d]pyrimidin-7-one Inhibitors of Cyclin-Dependent Kinases
AU Barvian, Mark; Boschelli, Dianne; Cossrow, Jennifer; Dobrusin, Ellen; Fattaey, Ali; Fritsch, Alex; Fry, David; Harvey, Patricia; Keller, Paul; Garrett, Michelle; La, Frances; Leopold, Wilbur; McNamara, Dennis; Quin, Marie; Trumpp-Kallmeyer, Susanne; Toogood, Peter; Wu, Zhipei; Zhang, Erli
CS Departments of Chemistry and Cancer Research, Parke-Davis Pharmaceutical Research Division of Warner Lambert Company, Ann Arbor, MI, 48105, USA
SO Journal of Medicinal Chemistry (**2000**), 43(24), 4606-4616
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 134:127686
AB The identification of 8-ethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one as an inhibitor of Cdk4 led to the initiation of a program to evaluate related pyrido[2,3-d]pyrimidin-7-ones for inhibition of cyclin-dependent kinases (Cdks). Anal. of more than 60 analogs has identified some clear SAR trends that may be exploited in the design of more potent Cdk inhibitors. The most potent Cdk4 inhibitors reported in this study inhibit Cdk4 with IC50 = 0.004 .mu.M ([ATP] = 25 .mu.M). X-ray crystallog. anal. of representative compds. bound to the related kinase, Cdk2, reveals that they occupy the ATP binding site. Modest selectivity between Cdks is exhibited by some compds., and Cdk4-selective inhibitors block pRb+ cells in the G1-phase of the cell division cycle.

IT **185040-35-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and structure-activity relationships of pyridopyrimidinone as inhibitors of cyclin-dependent kinases)

RN 185040-35-1 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)

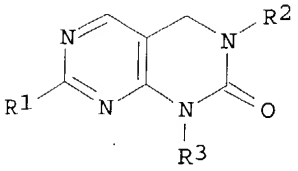


RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:291041 HCAPLUS
DN 132:308352
TI Preparation of pyrimidopyrimidinones as T-cell tyrosine kinase inhibitors
IN Harris, William; Hill, Christopher Huw; Smith, Ian Edward David
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000024744	A1	20000504	WO 1999-EP7675	19991013 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 9914677	A	20010717	BR 1999-14677	19991013 <--
	EP 1123295	A1	20010816	EP 1999-953796	19991013 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 200101102	T2	20020121	TR 2001-200101102	19991013 <--
	JP 2002528455	T2	20020903	JP 2000-578314	19991013 <--
	NZ 510760	A	20030829	NZ 1999-510760	19991013 <--
	AU 769989	B2	20040212	AU 2000-10363	19991013 <--
	US 6150373	A	20001121	US 1999-422451	19991021 <--
	ZA 2001002652	A	20020930	ZA 2001-2652	20010330 <--
	HR 2001000274	A1	20020630	HR 2001-274	20010412 <--
	NO 2001001929	A	20010419	NO 2001-1929	20010419 <--
PRAI	GB 1998-23277	A	19981023 <--		
	GB 1999-20044	A	19990824 <--		
	WO 1999-EP7675	W	19991013 <--		

OS MARPAT 132:308352
GI

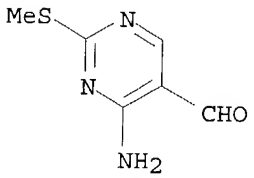


I

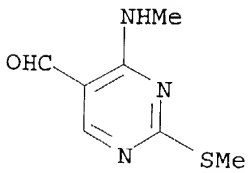
AB Title compds. [I; R1 = NH2, alkylamino, (hetero)aryl(alkyl)amino; R2 = alkyl (hetero)aryl(alkyl); R3 = H, alkyl, (hetero)aryl(alkyl), cycloalkenyl] were prepared Thus, Et 4-chloro-2-methylthiopyrimidine-5-carboxylate was aminated by MeNH2 and the product converted to the aldehyde which was condensed with 2,6-Cl2C6H3NH2 to give 2,6-Cl2C6H3NHCH2ZNHMe (Z = 2-methylthiopyrimidine-5,4-diyl). The latter was cyclocondensed with COCl2 and the the product oxidized to give I (R2 = 2,6-Cl2C6H3NHCH2, R3 = Me)(II; R1 = SO2Me) which was aminated by 4-(H2N)C6H4OCH2CH2NEt2 (preparation given) to give II [R1 = 4-(Et2NCH2CH2O)C6H4NH]. Data for biol. activity of I were given.

IT **770-31-0P 185040-32-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrimidopyrimidinones as T-cell tyrosine kinase inhibitors)

RN 770-31-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 185040-32-8 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:764041 HCAPLUS
DN 132:22971
TI Preparation of oxopyrido- and -pyrimidopyrimidines as cellular proliferation inhibitors
IN Dobrusin, Ellen Myra; Hamby, James Marino; Kramer, James Bernard; Schroeder, Mel Conrad; Showalter, Howard Daniel Hollis; Toogood, Peter;

Trumpp-Kallmeyer, Susanne A.
PA Warner-Lambert Co., USA
SO PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9961444	A2	19991202	WO 1999-US10187	19990510 <--
	WO 9961444	A3	20000203		
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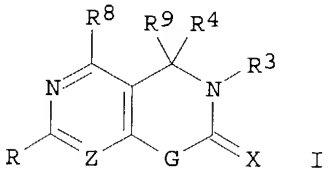
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2329703	AA	19991202	CA 1999-2329703	19990510 <--
	AU 9940734	A1	19991213	AU 1999-40734	19990510 <--
	AU 763839	B2	20030731		
	BR 9911590	A	20010213	BR 1999-11590	19990510 <--
	EP 1080092	A2	20010307	EP 1999-924165	19990510 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 200003429	T2	20010723	TR 2000-200003429	19990510 <--
	JP 2002516327	T2	20020604	JP 2000-550849	19990510 <--
	EE 200000706	A	20020617	EE 2000-706	19990510 <--
	NZ 508268	A	20040227	NZ 1999-508268	19990510 <--
	ZA 2000006536	A	20020211	ZA 2000-6536	20001110 <--
	BG 104960	A	20011031	BG 2000-104960	20001117 <--
	HR 2000000799	A1	20010630	HR 2000-799	20001120 <--
	NO 2000005928	A	20001123	NO 2000-5928	20001123 <--
	US 2004044012	A1	20040304	US 2003-638848	20030811 <--
PRAI	US 1998-86708P	P	19980526 <--		
	US 1999-126158P	P	19990325 <--		
	WO 1999-US10187	W	19990510 <--		
	US 2000-623737	A3	20000907 <--		

OS MARPAT 132:22971
GI



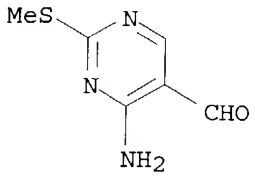
I

AB Title compds. [I; G = NR2 or CHR2; R = NHR1 or SO0-2R1; R1,R2 = H, (cyclo)alkyl, (un)substituted PH, -pyridyl, etc.; R3 = groups cited for R1, OH, alkoxy(carbonyl), etc.; R4 = H; R3R4 = bond; R8,R9 = H, halo, NH2, alkoxycarbonyl, etc.; X = O, S, (alkyl)imino, etc.; Z =N or CH] were prepared as cyclin-dependant and tyrosine kinase inhibitors. Thus, 5-aminomethyl-4-cyclopentylamino-2-methylthiopyrimidine (preparation given) was cyclocondensed with 1,1'-carbonyldiimidazole and the oxidized product aminated by 4-(MeO)C6H4NH2 to give I [G = cyclopentylimino, R = 4-(MeO)C6H4NH, R3 = R4 = R8 = R9 = H, X = O]. Data for biol. activity of

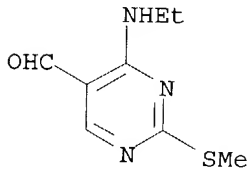
I were given.

IT **770-31-0 185040-35-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of bicyclic pyrimidines and bicyclic 3,4-dihydropyrimidines as inhibitors of cellular proliferation)

RN 770-31-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



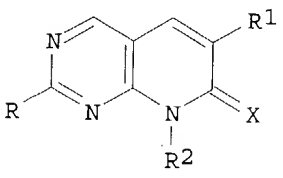
RN 185040-35-1 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



L44 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:561587 HCAPLUS
DN 131:184962
TI Preparation of oxidoamino-substituted pyrido[2,3-d]pyrimidines as protein tyrosine kinase inhibitors
IN Doherty, Annette Marian; Hallak, Hussein Osman; Hamby, James Marino
PA Warner-Lambert Company, USA
SO U.S., 25 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5945422	A	19990831	US 1998-15739	19980129 <--
PRAI US 1997-38822P	P	19970205 <--		

OS MARPAT 131:184962
GI



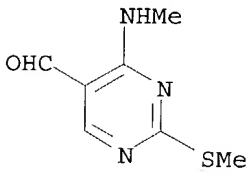
I

AB Title compds. [I;R = ONR5R6Z1Z2NH; R1 = (un)substituted Ph or heteroaryl; R2 = H, (cyclo)alkyl, phenyl(alkyl), heteroaryl, etc.; R5,R6 = H, alkyl, phenyl(alkyl), etc.; R5R6 = atoms to complete a ring; X = O, S, (acyl)imino; Z1,Z2 = bond, alkylene(oxy), -(thio), arylene] were prepared Thus, I (R1 = C6H3Cl2-2,6, R2 = Me, X = O)(II; R = SMe) was aminated by Et2NCH2CH2OC6H4(NH2)-4 and the product oxidized to give II [R = 4-(ONEt2CH2CH2O)C6H4NH]. Data for biol.activity of I were given.

IT **185040-32-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of oxidoamino-substituted pyrido[2,3-d]pyrimidines as protein tyrosine kinase inhibitors)

RN 185040-32-8 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



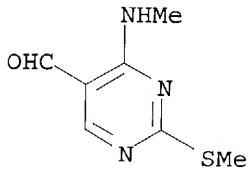
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:600713 HCAPLUS
DN 129:316187
TI Synthesis and Tyrosine Kinase Inhibitory Activity of a Series of 2-Amino-8H-pyrido[2,3-d]pyrimidines: Identification of Potent, Selective Platelet-Derived Growth Factor Receptor Tyrosine Kinase Inhibitors
AU Boschelli, Diane H.; Wu, Zhipei; Klutchko, Sylvester R.; Showalter, H. D. Hollis; Hamby, James M.; Lu, Gina H.; Major, Terry C.; Dahring, Tawny K.; Batley, Brian; Panek, Robert L.; Keiser, Joan; Hartl, Brian G.; Kraker, Alan J.; Klohs, Wayne D.; Roberts, Bill J.; Patmore, Sandra; Elliott, William L.; Steinkampf, Randy; Bradford, Laura A.; Hallak, Hussein; Doherty, Annette M.
CS Department of Medicinal Chemistry, Parke-Davis Pharmaceutical Research Division of Warner-Lambert Company, Ann Arbor, MI, 48105, USA
SO Journal of Medicinal Chemistry (**1998**), 41(22), 4365-4377
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Screening of a compound library led to the identification of 2-amino-6-(2,6-dichlorophenyl)-8-methylpyrido[2,3-d]pyrimidine (I) as a inhibitor of the platelet-derived growth factor receptor (PDGFr), fibroblast growth factor receptor (FGFr), and c-src tyrosine kinases (TKs). Replacement of the primary amino group at C-2 of I with a 4-(N,N-diethylaminoethoxy)phenylamino group gave a compound, which had greatly increased activity against all three TKs. In the present work, variation of the aromatic group at C-6 and of the alkyl group at N-8 of the pyrido[2,3-d]pyrimidine core provided several analogs that retained potency, including derivs. that were biased toward inhibition of the TK activity of PDGFr. Analogs of the 4-[(N,N-diethylaminoethoxy)phenylamino]-substituted derivative with a 3-thiophene or an unsubstituted Ph group at C-6

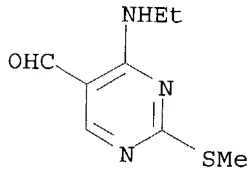
were the most potent inhibitors. One compound, 2-[4-[2-(diethylamino)ethoxy]phenylamino]-8-ethyl-6-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one had IC50 values of 31, 88, and 31 nM against PDGFr, FGFr, and c-src TK activity, resp.,. It was active in a variety of PDGF-dependent cellular assay and blocked the in vivo growth of three PDGF-dependent tumor lines.

IT **185040-32-8 185040-35-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and tyrosine kinase inhibitory activity of aminopyrido[2,3-d]pyrimidines)

RN 185040-32-8 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RN 185040-35-1 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:543072 HCAPLUS
DN 129:161569
TI Preparation of pyrido[2,3-d]pyrimidines and 4-aminopyrimidines as inhibitors of cellular proliferation
IN Boschelli, Diane Harris; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fattacy, Ali; Fry, David W.; Barvian, Mark R.; Kallmeyer, Susanne Trumpp; Wu, Zhipei
PA Warner Lambert Company, USA
SO PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9833798	A2	19980806	WO 1998-US1343	19980126 <--
	WO 9833798	A3	19981105		

W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU,

TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	AU 9866480	A1	19980825	AU 1998-66480	19980126 <--
	AU 749750	B2	20020704		
	EP 964864	A2	19991222	EP 1998-908442	19980126 <--
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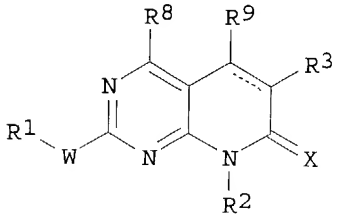
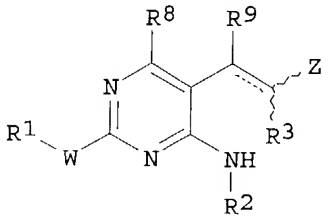
	BR 9807305	A	20000502	BR 1998-7305	19980126 <--
	NZ 335666	A	20001027	NZ 1998-335666	19980126 <--
	JP 2001509805	T2	20010724	JP 1998-532971	19980126 <--
	ZA 9800914	A	19981109	ZA 1998-914	19980204 <--
	US 6498163	B1	20021224	US 1999-355681	19990802 <--
PRAI	US 1997-37220P	P	19970205 <--		
	US 1997-69743P	P	19971216 <--		
	WO 1998-US1343	W	19980126 <--		

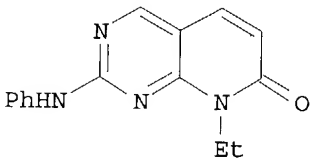
OS MARPAT 129:161569
GI



I



II



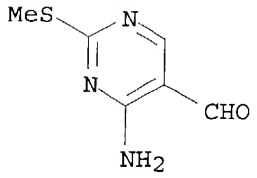
III

AB The title compds. [I and II; W = NH, S, SO, SO2; X = O, NH; R1, R2 = H, C1-10 alkyl, C3-10 cycloalkyl, etc.; R3 = H, alkyl; R8, R9 = H, C1-3 alkyl, OH, etc.; Z = CO2H] which inhibit a cyclin-dependent kinase (cdc2, cdk2, cdk4, cdk6) and a growth factor-mediated tyrosine kinase (FGF and PDGF) and therefore are useful for treating cell proliferatives disorders, such as cancer and restenosis, were prepared and formulated. Thus, treatment of Et 3-(4-ethylamino-2-phenylaminopyrimidin-5-yl)acrylate with 1,8-diazabicyclo[5.4.0]undec-7-ene in Et3N afforded the title compound III which showed IC50 of 0.41 and 0.752 .mu.M against cdk2/E and cdk4/D, resp.

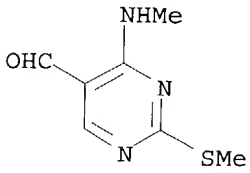
IT **770-31-0P 185040-32-8P 185040-35-1P 211247-46-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrido[2,3-d]pyrimidines and 4-aminopyrimidines as inhibitors of cellular proliferation)

RN 770-31-0 HCAPLUS

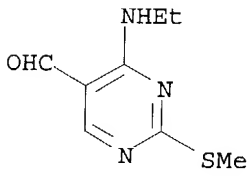
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



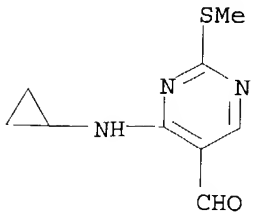
RN 185040-32-8 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RN 185040-35-1 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RN 211247-46-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(cyclopropylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



L44 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:496546 HCAPLUS
DN 129:211390
TI 2-Substituted Aminopyrido[2,3-d]pyrimidin-7(8H)-ones. Structure-Activity Relationships Against Selected Tyrosine Kinases and in Vitro and in Vivo Anticancer Activity

AU Klutchko, Sylvester R.; Hamby, James M.; Boschelli, Diane H.; Wu, Zhipei; Kraker, Alan J.; Amar, Aneesa M.; Hartl, Brian G.; Shen, Cynthia; Klohs, Wayne D.; Steinkampf, Randall W.; Driscoll, Denise L.; Nelson, James M.; Elliott, William L.; Roberts, Billy J.; Stoner, Chad L.; Vincent, Patrick W.; Dykes, Donald J.; Panek, Robert L.; Lu, Gina H.; Major, Terry C.; Dahring, Tawny K.; Hallak, Hussein; Bradford, Laura A.; Showalter, H. D. Hollis; Doherty, Annette M.

CS Departments of Chemistry Cancer Research Vascular and Cardiac Diseases and Pharmacokinetics and Drug Metabolism Parke-Davis Pharmaceutical Research Division, Warner-Lambert Company, Ann Arbor, MI, 48105, USA

SO Journal of Medicinal Chemistry (**1998**), 41(17), 3276-3292
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

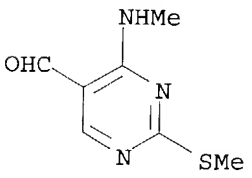
LA English

AB While engaged in therapeutic intervention against a number of proliferative diseases, we have discovered the 2-aminopyrido[2,3-d]pyrimidin-7(8H)-ones as a novel class of potent, broadly active tyrosine kinase (TK) inhibitors. An efficient route was developed that enabled the synthesis of a wide variety of analogs with substitution on several positions of the template. Compds. of this series were competitive with ATP and displayed submicromolar to low nanomolar potency against a panel of TKs, including receptor (platelet-derived growth factor, PDGFr; fibroblast growth factor, FGFr; epidermal growth factor, EGFr) and nonreceptor (c-Src) classes. One of the more thoroughly evaluated members was 63 with IC50 values of 0.079 .mu.M (PDGFr), 0.043 .mu.M (bFGFr), 0.044 .mu.M (EGFr), and 0.009 .mu.M (c-Src). In cellular studies, 63 inhibited PDGF-mediated receptor autophosphorylation in a number of cell lines at IC50 values of 0.026-0.002 .mu.M and proliferation of two PDGF-dependent lines at 0.3 .mu.M. It also caused inhibition of soft agar colony formation in three cell lines that overexpress the c-Src TK, with IC50 values of 0.33-1.8 .mu.M. In in vivo studies against a panel of seven xenograft tumor models with known and/or inferred dependence on the EGFr, PDGFr, and c-Src TKs, compound 63 produced a tumor growth delay of 10.6 days against the relatively refractory SK-OV-3 ovarian xenograft and also displayed activity against the HT-29 tumor. In rat oral bioavailability studies, compound 63 plasma concns. declined in a biexponential manner, and systemic plasma clearance was high relative to liver blood flow. Finally, in rat metabolism studies, HPLC chromatog. identified two metabolites of 63. Because of the excellent potency of 63 against selected TKs, in vitro and in vivo studies are underway for this compound in addnl. tumor models dependent upon PDGFr, FGFr, and c-Src to assess its potential for advancement to clin. trials.

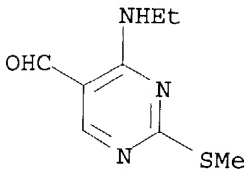
IT **185040-32-8P 185040-35-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminopyridopyrimidinones as tyrosine kinase inhibitors and anticancer agents)

RN 185040-32-8 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RN 185040-35-1 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)

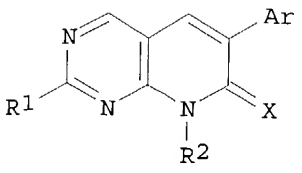


RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:202673 HCAPLUS
DN 128:257440
TI Preparation of pyrido[2,3-d]pyrimidines for inhibiting protein tyrosine kinase mediated cellular proliferation
IN Blankley, Clifton John; Boschelli, Diane Harris; Doherty, Annette Marian; Hamby, James Marino; Klutchko, Sylvester; Panek, Robert Lee
PA Warner-Lambert Company, USA
SO U.S., 39 pp., Cont.-in-part of U.S. 5,620,981.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5733914	A	19980331	US 1996-611279	19960403 <--
	US 5620981	A	19970415	US 1995-433294	19950503 <--
	IL 117923	A1	20000601	IL 1996-117923	19960416 <--
	CA 2214219	AA	19961107	CA 1996-2214219	19960426 <--
	WO 9634867	A1	19961107	WO 1996-US5819	19960426 <--
	W: AU, BG, CA, CN, CZ, EE, GE, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, UZ, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9655769	A1	19961121	AU 1996-55769	19960426 <--
	AU 713727	B2	19991209		
	EP 823908	A1	19980218	EP 1996-913175	19960426 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
	CN 1183099	A	19980527	CN 1996-193678	19960426 <--
	CN 1083452	B	20020424		
	JP 11504922	T2	19990511	JP 1996-533372	19960426 <--
	NZ 307021	A	20010427	NZ 1996-307021	19960426 <--
	CZ 288160	B6	20010516	CZ 1997-3275	19960426 <--
	EE 3770	B1	20020617	EE 1997-274	19960426 <--
	PL 184093	B1	20020830	PL 1996-323089	19960426 <--
	SK 283952	B6	20040608	SK 1997-1410	19960426 <--
	ZA 9603486	A	19961113	ZA 1996-3486	19960502 <--
	NO 9705033	A	19971031	NO 1997-5033	19971031 <--
PRAI	US 1995-433294	A2	19950503 <--		
	US 1996-611279	A	19960403 <--		
	WO 1996-US5819	W	19960426 <--		

OS MARPAT 128:257440
GI

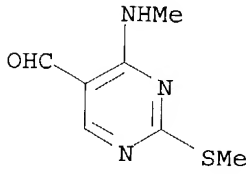


I

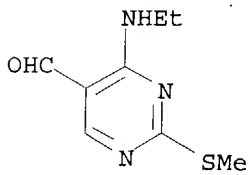
AB The title compds. [I; X = NH, N-acyl, O, S; R1 = SOR3, SO2R3; R2, R3 = H, (CH2)nPh (where Ph = (un)substituted phenyl; n = 0-3), heteroarom., etc.; Ar = (un)substituted Ph, heteroaryl], inhibitors of protein tyrosine kinases, and thus useful in treating cellular proliferation, especially useful in treating cancer, atherosclerosis, restenosis, and psoriasis, were prepared and formulated. Thus, treatment of 2-ethoxyethanol with NaH followed by addition of 2,6-dimethylphenylacetonitrile, and 2-amino-4-methylamino-5-pyrimidinecarboxaldehyde (preparation described) afforded pyrido[2,3-d]pyrimidine I [R1 = NH2; R2 = Me; X = NH; Ar = 2,6-dimethylphenyl] which showed 42% inhibition of PDGFr-TK at 50 .mu.M.

IT **185040-32-8P 185040-35-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrido[2,3-d]pyrimidines for inhibiting protein tyrosine kinase mediated cellular proliferation)

RN 185040-32-8 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RN 185040-35-1 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:202672 HCAPLUS
DN 128:257439
TI Preparation of 6-arylpyrido[2,3-d]pyrimidines and naphthyridines for

inhibiting protein tyrosine kinase mediated cellular proliferation

IN Blankley, Clifton John; Doherty, Annette Marian; Hamby, James Marino; Panek, Robert Lee; Schroeder, Mel Conrad; Showalter, Howard Daniel Hollis; Connolly, Cleo

PA USA

SO U.S., 36 pp., Cont.-in-part of U.S. Ser. No. 339,051, abandoned.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5733913	A	19980331	US 1995-539410	19951106 <--
	CA 2199964	AA	19960523	CA 1995-2199964	19951113 <--
	WO 9615128	A2	19960523	WO 1995-US14700	19951113 <--
	W: AM, AU, BG, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, UA, UZ				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9641078	A1	19960606	AU 1996-41078	19951113 <--
	AU 711426	B2	19991014		
	EP 790997	A2	19970827	EP 1995-939129	19951113 <--
	EP 790997	B1	20000322		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	HU 76853	A2	19971229	HU 1997-1511	19951113 <--
	CN 1169726	A	19980107	CN 1995-196230	19951113 <--
	CN 1085666	B	20020529		
	JP 10509452	T2	19980914	JP 1995-516240	19951113 <--
	CZ 286160	B6	20000112	CZ 1997-1390	19951113 <--
	AT 190978	E	20000415	AT 1995-939129	19951113 <--
	PT 790997	T	20000630	PT 1995-939129	19951113 <--
	ES 2146782	T3	20000816	ES 1995-939129	19951113 <--
	SK 281724	B6	20010710	SK 1997-609	19951113 <--
	PL 181893	B1	20011031	PL 1995-320169	19951113 <--
	MD 1861	F2	20020228	MD 1997-970187	19951113 <--
	RU 2191188	C2	20021020	RU 1997-110269	19951113 <--
	ZA 9509675	A	19960529	ZA 1995-9675	19951114 <--
	IL 115970	A1	19990620	IL 1995-115970	19951114 <--
	BG 63162	B1	20010531	BG 1997-101326	19970313 <--
	FI 9701953	A	19970512	FI 1997-1953	19970507 <--
	NO 9702198	A	19970513	NO 1997-2198	19970513 <--
	US 5952342	A	19990914	US 1998-40792	19980318 <--
	GR 3033439	T3	20000929	GR 2000-401126	20000518 <--
PRAI	US 1994-339051	B2	19941114 <--		
	US 1995-539410	A	19951106 <--		
	WO 1995-US14700	W	19951113 <--		

OS MARPAT 128:257439

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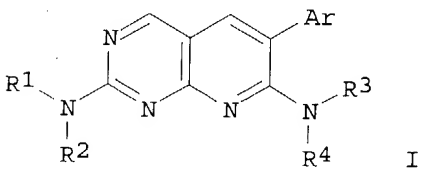


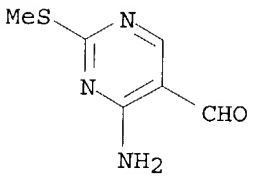
I

AB The title compds. [I; R1, R2, R4 = H, C1-8 alkyl, C2-8 alkenyl, etc.; R3 = C(O)R8, CO2R8, C(S)R8, etc.; R8 = H, C1-8 alkyl, C2-8 alkenyl, etc.; Ar =

(un)substituted aromatic ot heteroarom. selected from Ph, imidazolyl, pyrrolyl, etc.], inhibitors of protein tyrosine kinase which are especially useful in treating atherosclerosis, restenosis, psoriasis, as well as bacterial infections, were prepared and formulated. Thus, reaction of 2,7-diamino-6-(2,6-dichlorophenyl)pyrido[2,3-d]pyrimidine (preparation described) with tert-Bu isocyanate in the presence of NaH in DMF afforded the urea I [R1 = R4 = H; R2 = R3 = C(O)NHtBu; Ar = 2,6-Cl2C6H3] which showed IC50 of 10.2 .mu.M against PDGF receptor tyrosine kinase.

IT **770-31-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 6-arylpyrido[2,3-d]pyrimidines and naphthyridines for inhibiting protein tyrosine kinase mediated cellular proliferation)

RN 770-31-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



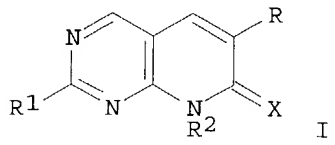
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:26258 HCAPLUS
DN 126:59965
TI Preparation of pyrido[2,3-d]pyrimidines as protein tyrosine kinase mediated cell proliferation inhibitors
IN Blankley, Clifton John; Boschelli, Diane Harris; Doherty, Annette Marian; Hamby, James Marino; Klutchko, Sylvester; Panek, Robert Lee
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9634867	A1	19961107	WO 1996-US5819	19960426 <--
	W: AU, BG, CA, CN, CZ, EE, GE, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, UZ, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5620981	A	19970415	US 1995-433294	19950503 <--
	US 5733914	A	19980331	US 1996-611279	19960403 <--
	AU 9655769	A1	19961121	AU 1996-55769	19960426 <--
	AU 713727	B2	19991209		
	EP 823908	A1	19980218	EP 1996-913175	19960426 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
	JP 11504922	T2	19990511	JP 1996-533372	19960426 <--
	NZ 307021	A	20010427	NZ 1996-307021	19960426 <--
	EE 3770	B1	20020617	EE 1997-274	19960426 <--
	PL 184093	B1	20020830	PL 1996-323089	19960426 <--
	SK 283952	B6	20040608	SK 1997-1410	19960426 <--

	NO 9705033	A	19971031	NO 1997-5033	19971031 <--
PRAI	US 1995-433294	A	19950503	<--	
	US 1996-611279	A	19960403	<--	
	WO 1996-US5819	W	19960426	<--	

OS MARPAT 126:59965
GI

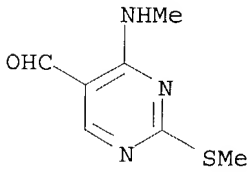


I

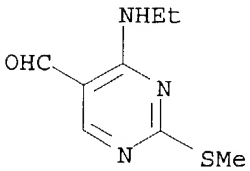
AB Title compds. [I; R = (un)substituted Ph or heteroaryl; R1 = NR3R4, SO0-2R3, OR3; R2-R4 = H, alkyl, (CH2)0-3Ph, heteroaryl, etc.; R4 may addnl. = COR3, CO2R3, SO2R3, etc.; NR3R4 = atoms to form a ring; X = O, S, (acyl)imino] were pred. Thus, EtOCH:C(CN)CO2Et was cyclocondensed with MeSC(:NH)NH2 and the product converted in 5 steps to 2-amino-4-methylamino-5-pyrimidinecarboxaldehyde which was cyclocondensed with 2,6-Me2C6H3CH2CN to give I (R = 2,6-Me2C6H3, R1 = NH2, R2 = Me, X = NH). Data for biol. activity of I were given.

IT **185040-32-8P 185040-35-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrido[2,3-d]pyrimidines as protein tyrosine kinase mediated cell proliferation inhibitors)

RN 185040-32-8 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(methylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RN 185040-35-1 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



L44 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:467130 HCAPLUS
DN 125:114688
TI Preparation of 6-aryl pyrido[2,3-d]pyrimidines and naphthyridines for

inhibiting protein tyrosine kinase-mediated cellular proliferation

IN Blankley, Clifton John; Doherty, Annette Marian; Hamby, James Marino; Panek, Robert Lee; Schroeder, Mel Conrad; Showalter, Howard Daniel Hollis; Connolly, Cleo

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 134 pp.
CODEN: PIXXD2

DT Patent

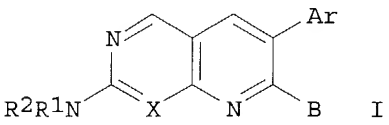
LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9615128	A2	19960523	WO 1995-US14700	19951113 <--
	W: AM, AU, BG, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, UA, UZ				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5733913	A	19980331	US 1995-539410	19951106 <--
	AU 9641078	A1	19960606	AU 1996-41078	19951113 <--
	AU 711426	B2	19991014		
	EP 790997	A2	19970827	EP 1995-939129	19951113 <--
	EP 790997	B1	20000322		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10509452	T2	19980914	JP 1995-516240	19951113 <--
	AT 190978	E	20000415	AT 1995-939129	19951113 <--
	SK 281724	B6	20010710	SK 1997-609	19951113 <--
	PL 181893	B1	20011031	PL 1995-320169	19951113 <--
	MD 1861	F2	20020228	MD 1997-970187	19951113 <--
	RU 2191188	C2	20021020	RU 1997-110269	19951113 <--
	BG 63162	B1	20010531	BG 1997-101326	19970313 <--
	FI 9701953	A	19970512	FI 1997-1953	19970507 <--
	NO 9702198	A	19970513	NO 1997-2198	19970513 <--
	GR 3033439	T3	20000929	GR 2000-401126	20000518 <--
PRAI	US 1994-339051	A	19941114 <--		
	US 1995-539410	A	19951106 <--		
	WO 1995-US14700	W	19951113 <--		

OS MARPAT 125:114688

GI



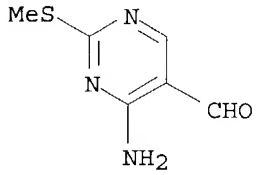
I

AB 6-Arylpyrido[2,3-d]pyrimidines and naphthyridines I [X = CH, N; B = halo, OH, NR3R4; R1, R2, R3, R4 = H, C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, Ar', amino, C1-8 alkylamino, di-C1-8 alkylamino, wherein the alkyl, alkenyl, and alkynyl groups may be substituted by amino, OH, or 5- or 6-membered carbocyclic or heterocyclic ring; Ar, Ar' = (un)substituted aromatic or heteroarom. groups; R1R2N or R3R4N can complete a ring having 3-6 C atoms and optionally containing 1 or 2 heteroatoms; when X = N and B = NR3R4, one of R3 and R4 .noteq. H] or their pharmaceutically acceptable acid and base addition salts, useful as inhibitors of protein tyrosine kinase and thus useful in treating cellular proliferation mediated thereby, are claimed. The compds. are especially useful in treating atherosclerosis, restenosis, psoriasis, as well as bacterial infections. In an example, the IC50 of I [X = N, B = NHCONH2, R1 = H, R2 = Et2N(CH2)4 Ar = 2,6-Cl2C6H3; preparation given] for inhibition of protein tyrosine kinases was

0.231 .mu.M for PDGF and 0.0954 for FGF.

IT **770-31-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aryl pyridopyrimidines and naphthyridines for inhibiting protein tyrosine kinase-mediated cellular proliferation)

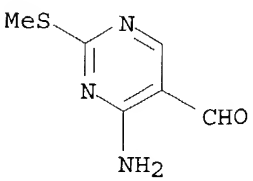
RN 770-31-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



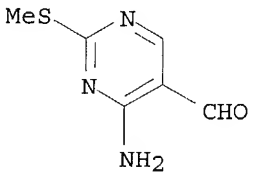
L44 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1965:10720 HCAPLUS
DN 62:10720
OREF 62:1994f-h
TI Bacterial synthesis and destruction of thiamine. V. Effects of 2-alkylthiothiamine and their pyrimidine moiety derivatives on the growth and thiamine synthesis of bacteria
AU Ogata, Juichi
CS Yamaguchi Med. School, Ube, Japan
SO Bitamin (**1959**), 18(3), 591-8
CODEN: BTMNA7; ISSN: 0006-386X
DT Journal
LA Unavailable
AB 2-Methylthiothiamine was an inhibitory antagonist against a thiamine-requiring mutant of Escherichia coli strain 70-23 and the molar ratio of inhibition (inhibitor/thiamine) was of the order of 100-1000. The corresponding 2-ethylthiothiamine showed much less inhibitory potency than the Me derivative in the same molar ratio. On the other hand, a thiamine-pyrimidine-requiring mutant strain 70-17 could use the Me derivative alone for growth in place of pyrimidine at concns. 10-6 moles/l. The mutant was, however, inhibited by the compound in the presence of <10-9 moles/l. of thiamine. The pyrimidine moiety of this compound did not have inhibitory activity for both strains and was utilized for synthesis of the compound by the parent strain ATCC 9637. It was, therefore, probable that the compound was competitive for thiamine at the stage of phosphorylation of thiamine or later.

IT **770-31-0**, 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)-
(effect on thiamine formation by Escherichia coli)

RN 770-31-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



L44 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1965:10719 HCAPLUS
DN 62:10719
OREF 62:**1994e-f**
TI Bacterial synthesis and destruction of thiamine. IV. Destruction of 2-methylthiothiamine by thiaminase and inhibitory effect of the pyrimidine moiety
AU Ogata, Juichi
CS Yamaguchi Med. School, Ube, Japan
SO Bitamin (**1959**), 18(2), 460-3
CODEN: BTMNA7; ISSN: 0006-386X
DT Journal
LA Unavailable
AB cf. CA 56, 9200f. Evidence was presented to show that the thiaminase of Bacillus aneurinolyticus actually hydrolyzes the 2-methylthio analog of thiamine. The degradation products were identified by separating them by paper chromatography and measuring an uv absorption spectrum of the separated compds. The hydrolysis of this compound was inhibited by thiamine pyrimidine more markedly than thiamine, and by thiamine thiazole which acted on thiamine only slightly. The hydrolysis of 2-methylthiothiamine was also inhibited by a high concentration of the pyrimidine moiety of this compound 2-Methylthiothiamine was also decomposed by the staphylococcal extract
However, several pyrimidyl compds. revealed inhibitory effects against the decomposition
IT **770-31-0**, 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)-
(effect on 2-(methylthio)thiamine hydrolysis by thiaminase of Bacillus aneurinolyticus)
RN 770-31-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



L44 ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1965:10718 HCAPLUS
DN 62:10718
OREF 62:**1994d-e**
TI Microbiological evaluation of triacetyloleandomycin(TAO)
AU Vakulenko, N. A.
SO Antibiotiki (1964), 9(11), 1017-20
DT Journal
LA Russian
AB TAO had a high antibiotic activity on gram-pos. bacteria and staphylococci resistant to other antibiotics. It has no effect on gram-neg. bacteria. Its high level in blood indicates fast absorption. Its activity can be tested by diffusion in agar, utilizing Bacillus subtilis. Its diffusion rate is linear in the range of 10-50 units/cc.; it is soluble and stable in 0.01N HCL.

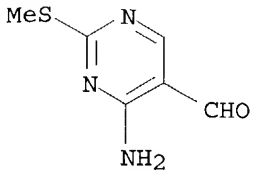
L44 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1964:18925 HCAPLUS
DN 60:18925
OREF 60:**3376d-e**
TI Cancer chemotherapy screening data. XXV. Sarcoma 180 screening data
AU Reilly, H. Christine; Falco, Elvira; Myron, Sophronia A.; Philips, Frederick S.; Stock, C. Chester
CS Cornell Univ., New York, NY
SO Cancer Research (1963), 23(9;Pt. 2), 1731-1877
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA Unavailable
AB Unavailable

L44 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1964:18924 HCAPLUS
DN 60:18924
OREF 60:**3376d**
TI Cancer chemotherapy screening data. XXIV. A mitomycin C-resistant Jensen rat sarcoma; chemotherapy studies
AU Sugiura, Kanematsu; Merker, Philip C.
CS Cornell Univ., New York, NY
SO Cancer Research (1963), 23(8;Pt. 2), 1475-82
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA Unavailable
AB Unavailable

L44 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1964:18923 HCAPLUS
DN 60:18923
OREF 60:**3376d**
TI Cancer chemotherapy screening data. XXIII. Microbiological screening of chemicals for potential antitumor activity
AU Scott, D. B. McNair; Batcheler, M. L. Rogers; Lesher, E. Chu; Pakoskey, A. M.
CS Univ. of Pennsylvania, Philadelphia
SO Cancer Research (1963), 23(7;Pt. 2), 1235-77
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA Unavailable
AB Unavailable

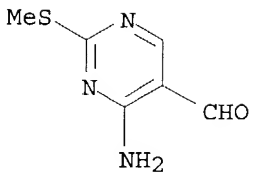
L44 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1964:18922 HCAPLUS
DN 60:18922
OREF 60:**3376c-d**
TI Cancer chemotherapy screening data. XXI. Patterns of response of animal tumors to anticancer agents. A systematic analysis of the literature in experimental cancer chemotherapy 1945-1958
AU Hirschberg, Erich
CS Columbia Univ.
SO Cancer Research (**1963**), 23(Suppl.;5;Pt. 2), 521-980
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA Unavailable
AB cf. CA 60, 995d. This indexed compilation contains information concerning 626 compds. tested. 2291 references.
IT **770-31-0**, 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)-
(bacterial response to, neoplasm inhibition and)

RN 770-31-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



L44 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1960:12238 HCAPLUS
DN 54:12238
OREF 54:**2530c-e**
TI Influence of nicotinic acid on hepatic cholesterol synthesis in rabbits
AU Schade, Hugh; Saltman, Paul
CS Univ. of S. California, Los Angeles
SO Proceedings of the Society for Experimental Biology and Medicine (1959), 102, 265-7
CODEN: PSEBAA; ISSN: 0037-9727
DT Journal
LA Unavailable
AB Ingestion of large amts. of nicotinic acid (I) is known to lower serum cholesterol in rabbits. The rate at which cholesterol is synthesized from acetate-1-C14 by liver slices from rabbits on control or cholesterol supplemented diets, with or without I, was measured. The rate was markedly lowered by I ingestion. Since the principal detoxication product of large doses of I is nicotinuric acid, it is possible that this inhibition of cholesterol synthesis may be a direct result of competition of lipide-synthesizing and detoxication systems for a limiting quantity of coenzyme A in the liver cell.

L44 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1960:12237 HCAPLUS
DN 54:12237
OREF 54:**2530b-c**
TI Metabolic alteration of 2-methylthio-4-amino-5-hydroxymethylpyrimidine (methioprim)
AU Slotnick, Irving J.; Spears, Alexander W.; Tieckelmann, Howard
CS Univ. of Buffalo, Buffalo, NY
SO Proceedings of the Society for Experimental Biology and Medicine (**1959**), 102, 239-42
CODEN: PSEBAA; ISSN: 0037-9727
DT Journal
LA Unavailable
AB Rat liver slices oxidize the 5-CH2OH group partly to 5-CHO and partly to 5-COOH. Another unidentified ultraviolet-absorbing substance also is produced. The antibacterial activity of the 5-CHO derivative is less than that of methioprim, and the 5-COOH derivative is inactive.
IT **770-31-0**, 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (formation from methioprim metabolism and its bactericidal action)
RN 770-31-0 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



L44 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1959:122257 HCAPLUS
DN 53:122257
OREF 53:**21999g-i,22000a-i,22001a-e**
TI Some analogs of toxopyrimidine and methioprim
AU Okuda, Takuo; Price, Charles C.
CS Univ. of Pennsylvania, Philadelphia
SO Journal of Organic Chemistry (**1958**), 23, 1738-41
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA Unavailable
GI For diagram(s), see printed CA Issue.
AB A number of new pyrimidines, related to toxopyrimidine, N:CMe.N:C(NH2).C(CH2X):CH (I) (X = OH) (II), having antimetabolite properties, and methioprim, N:C(SR).N:C(NH2).C(CH2X):CH (III) (R = Me, X = OH) (IV), having anti-metabolite and antitumor activity, were prepared I (X = Br) di-HBr salt (V) (30 g.) slowly added to 6.3 g. AcSH in 150 ml. C5H5N, after the evolution of heat stopped the mixture stirred and refluxed gently 7 hrs., cooled, the precipitate filtered off, washed with Et2O, dissolved in 35 ml. 5% HCl, the solution washed with Et2O, made weakly alkaline with aqueous Na2CO3, extracted quickly 10 times with 100 ml. portions Et2O, the combined exts. dried, the Et2O distilled in vacuo, and the residual product (3.0 g.) recrystd. 3 times (Me2CO) gave I (X = SH) (VI), m. 161-3.degree.; the aqueous alkaline solution from which VI had been extracted kept 4 days at room temperature and the precipitate (1.6 g.) which separated recrystd. (EtOH) gave bis(2-methyl-4-amino-5-pyrimidylmethyl) disulfide (VII), m. 242-5.degree. (decomposition). V (10 g.) added to 2.08 g. thiourea in 150 ml. tetrahydrofuran (VIII), the mixture refluxed and stirred 50 min., cooled, and the precipitate (IX) (11.6 g.) collected, IX (5 g.) dissolved in 50 ml. 10% aqueous NaOH, the solution neutralized with HCl after standing 30 min., extracted 5 times with 100 ml. portions Et2O, the combined exts. dried, the Et2O distilled, and the residual material (100 mg.) recrystd. twice (20 ml. portions EtOH) gave VII, m. 245.degree., mixed m.p. not depressed; the neutralized solution above after Et2O extraction concentrated in vacuo to 10 ml., cooled, the precipitate collected, and recrystd. 3 times (EtOH) gave 7-amino-2-methyl-5(H)-m-thiazino-[4,5-d]pyrimidine (X), N:CMe.N:CH.C:C.N:C(NH2).S.CH2, m. 256-8.degree.. IX (5 g.) dissolved in 30 ml. H2O, the solution made weakly alkaline with Na2CO3, the precipitate collected, washed 3 times with 10 ml. portions H2O, treated with 500 ml. EtOH (the precipitate slowly dissolved with NH3 evolution), the solution concentrated to 50 ml., cooled, and the separated crystals (1.78 g.) recrystd. (80 ml. EtOH) gave X, m.p. and mixed m.p. 256-8.degree.. IX (11.6 g.) dissolved in 15 ml. H2O, neutralized with NaOH, the precipitate (5.4 g.) collected, washed with 10 ml. H2O, dissolved in 30 ml. boiling 10% aqueous NaOH, the solution refluxed 1 hr., cooled, and the precipitate recrystd. (EtOH) gave 1.3 g.

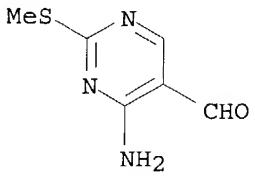
bis(2-methyl-4-amino-5-pyrimidylmethyl) sulfide (XI), m. 284-6.degree. (decomposition). MeSH (10 g.) added to 3.8 g. Na in 150 ml. absolute EtOH followed by 20 g. V, the mixture stirred and refluxed 30 min., cooled, and the precipitate (23 g.) recrystd. (1st from 100 ml. 50% EtOH, and then 50 ml. 50% EtOH) gave 4.0 g. I (X = SMe), m. 176-8.degree.; concentration of the mother liquors yielded an addnl. 2.5g. Na (2 g.) added to 5 g. MeSH in 100 ml. Et2O cooled in an ice salt bath, after stirring 4 hrs. 10 g. V added (no heat evolved), the Et2O and excess MeSH distilled, the residue heated with 50 ml. dioxane on a steam bath, the mixture heated and stirred 1 hr., the solid filtered off, cooled, 10 ml. EtOH added, the solvent distilled, 50 ml. H2O added, and the solid (0.4 g.) recrystd. (50 ml. EtOH) gave XI. V (5 g.) added to 1.35 g. KSCN in 150 ml. VIII, the mixture refluxed and stirred 2 hrs., cooled, the precipitate (3 g.) collected, dissolved in 25 ml. H2O, the solution neutralized with NaHCO3, and the precipitate (0.9 g.) recrystd. 3 times (C6H6 gave I (X = SCN) (XII), decompose 150-98.degree.; the filtrate from XII concentrated to 10 ml., kept overnight, and the precipitate (0.3 g.) recrystd. (EtOH) gave VII. IV (5 g.) in 13 ml. AcOH added with stirring to 2.9 g. Na2Cr2O7.2H2O in 15 ml. AcOH, after 2 hrs. the precipitate (XIII) (3.4 g.) collected, and washed with 30 ml. H2O, the cooled filtrate neutralized with NH4OH, kept overnight at 0.degree., the precipitate (0.7 g.) combined with XIII, dissolved in 300 ml. CHCl3, the solution washed twice with 20 ml. portions H2O, dried, concentrated to 100 ml., cooled, and the product filtered off gave 2.50 g. 2-methylthio-4-amino-5-formylpyrimidine (XIV), m. 183-4.degree. (concentration of the filtrate to 20 ml. yielded an addnl. 0.50 g., m. 182-3.degree.); oxime, m. 201-2.degree. (C6H6EtOH). To 5 g. LiAlH4 in 50 ml. anhydrous Et2O and 300 ml. O.CH2.CH2.NEt.CH2.CH2 was slowly added 10 g. finely powdered N:C(SH).N:C(NH2).C(CO2Et):CH (XV), after the evolution of heat ceased the mixture heated and stirred 2.5 hrs. at 80.degree., cooled, 20 ml. EtOAc added followed by 10 ml. H2O, kept overnight, the precipitate filtered off (no crystalline material in the filtrate), extracted (Soxhlet) with boiling EtOH, the extract concentrated to 20 ml., neutralized with AcOH, and the precipitate (3.8 g.) recrystd. 4 times (EtOH) to give III (R = H, X = OH), m. 229-32.degree. (decomposition). AcOH (175 ml.) saturated with anhydrous HBr at 0.degree. added to 12 g. IV in 100 ml. AcOH, heated 2 hrs. on a steam bath, cooled, the precipitate (27.5 g.) collected, and recrystd. (650 ml. AcOH) gave 18.5 g. III (R = Me, X = Br) HBr salt (XVI), decompose above 280.degree.. XVI (2 g.) refluxed 1 hr. with 20 ml. MeOH, the MeOH distilled, aqueous NH3 added to the oily residue until the solution became weakly alkaline, cooled, and the precipitate (0.7 g.) recrystd. (H2O and then C6H6-ligroine) gave III (R = Me, X = OMe), m. 104-6.degree.. MeSH (1 g.) added to 0.5 g. Na in 100 ml. absolute EtOH followed by 3 g. XVI with stirring, after evolution of heat stopped the mixture heated 30 min. on a steam bath with stirring, the EtOH distilled, 40 ml. H2O added to the residue, the mixture stirred and heated 10 min., cooled, the precipitate filtered off, and recrystd. twice (30% EtOH) gave 1.4 g. III (R = Me, X = SMe), m. 139-40.degree.. XVI (4 g.) added to 2 g. AcSH in 25 ml. C5H5N, the mixture stirred and heated 1 hr. on a steam bath, the C5H5N distilled in vacuo, the residue dissolved in 20 ml. H2O.2% aqueous NaOH added to the solution until it was weakly alkaline, the solid filtered off, and recrystd. (EtOH) gave 1.8 g. III (R = Me, X = SAc), m. 161-3.degree. (EtOH, then ligroine-C6H6). XVI (5.4 g.) added to 2.7 g.

AcSH in 25 ml. C5H5N, the mixture heated 1 hr. on a steam bath, cooled, the precipitate filtered off, the filtrate distilled in vacuo, the viscous residue heated 1 hr. on a steam bath with 30 ml. 2% HCl, the resulting solution neutralized with Na2CO3, cooled, the precipitate filtered off (no crystalline product obtained from this precipitate), the filtrate extracted with Et2O, the combined exts. dried, the Et2O distilled, C5H5N removed in vacuo, and the residue (99.6 mg.) recrystd. (C6H6) gave III (R = Me, X = SH) (XVII), m. 138-9.degree.. XVI (5 g.) added to 1.3 g. thi.ANG.ourea in 100 ml. Me2CO, the mixture refluxed and stirred 2 hrs., cooled, the precipitate (4.5 g.) collected, and recrystd. (EtOH) gave III [R = Me, X = SC(NH2)2Br] HBr salt (XVIII), m. 240-1.degree.. XVIII (3 g.) in 40 ml. H2O adjusted to pH 8 with NH4OH and the precipitate (XIX) (1.25 g.) (m. 103-5.degree.) collected, XIX (0.2 g.) dissolved in 20 ml. boiling EtOH, the solution concentrated to 2 ml., cooled overnight, and the precipitate recrystd. (EtOH) gave bis(2-methylthio-4-amino-5-pyrimidylmethyl) disulfide, m. 213-15.degree.; the filtrate after standing 5 days at room temperature deposited an addnl. 0.15 g. XV (10 g.) in 3.1 g. KOH in 50 ml. H2O treated gradually with 8 g. Et2SO4 with shaking, stirred 3 hrs., the precipitate collected, washed, and dried gave 9.4 g. 2-EtS compound (XX), m. 100-2.degree. (EtOH). XX placed in a Soxhlet extractor mounted on a flask containing 3 g. LiAlH4 in 350 ml. dry Et2O, the Et2O refluxed and stirred 3 hrs., cooled, 20 ml. EtOAc added with stirring followed by 10 ml. H2O, the mixture let stand overnight, the precipitate filtered off, extracted 3 times with 100 ml. portions boiling Me2CO, the Me2CO exts. combined, and the Me2CO distilled, the Et2O distilled from the filtrate, the residues combined, washed with Me2CO and C5H5, and recrystd. (EtOH) gave 5.9 g. III (R = Et, X = OH), m. 154-5.5.degree.. The infrared characteristics of X, XI, and XII are recorded. IV, XIV, XVI, and XVII are antagonists for II in microorganisms requiring II for growth.

IT **770-31-0**, 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (preparation of)

RN 770-31-0 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



L44 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1959:122256 HCAPLUS

DN 53:122256

OREF 53:**21999d-g**

TI Hydrolysis and alcoholysis of quinazoline-2-carbonitrile derivatives

AU Higashino, Takeo

CS Shizuoka Coll. Pharm.

SO Yakugaku Zasshi (1959), 79, 702-5
CODEN: YKKZAJ; ISSN: 0031-6903

DT Journal

LA Unavailable
AB 4-(RO-substituted)quinazoline-2-carbonitrile (I, R = Me, Et, Bu, and PhCH2) (0.5 g.) in 3 ml. 30% H2O2 and 20 ml. Me2CO made alk by adding 10% K2CO3 dropwise, kept overnight, and the Me2CO removed gave 4-(RO-substituted)quinazoline-2-carboxamide (II) (R, % yield, and m.p. given): Me, 74, 204-6.degree.; Et, 74, 183-4.degree.; Bu, 78, 148-50.degree.; PhCH2, 75, 156-7.degree.. I (R = Et and Bu) or 4-NCC9H6N (0.5 g.) in 25 ml. EtOH (CHCl3 added in case of insoly. in EtOH) saturated with HCl gas, kept overnight, the EtOH removed in vacuo, the residue in 15 ml. H2O kept 1 hr., neutralized with K2CO3, extracted with CHCl3, the CHCl3 removed, and the residue taken up in C6H6 gave hygroscopic crystals of Et 4-(RO-substituted)quinazoline-2-carboxylate or 4-EtO2CC9H6N, and the C6H6-insol. portion gave the corresponding amides. The above reaction in alkali gave more yield of the ester and less amide. Et 4-ethoxyquinazoline-2-carboxylate in EtOH and 80% N2H4.H2O heated 10 min. on a H2O bath and the EtOH removed gave 4-ethoxyquinazoline-2-carbohydrazide, m. 203-4.degree.. Similarly were prepared 2-H2NNHOCC9H6N, m. 140-1.degree., and 4-H2NNHOCC9H6N, m. 137-9.degree.. PhCN (0.5 g.) in 25 ml. EtOH saturated with HCl gas, the solution concentrated, the residue extracted with Et2O and H2O, and the Et2O layer concentrated yielded 39% BzOEt; the H2O layer yielded 37% BzNH2.

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DICTIONARY FILE UPDATES:    3 AUG 2004  HIGHEST RN 721883-12-1

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http://www.cas.org/ONLINE/DBSS/registryss.html

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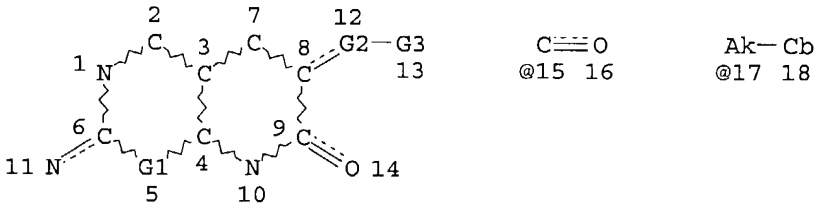


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DEFAULT ECLEVEL IS LIMITED

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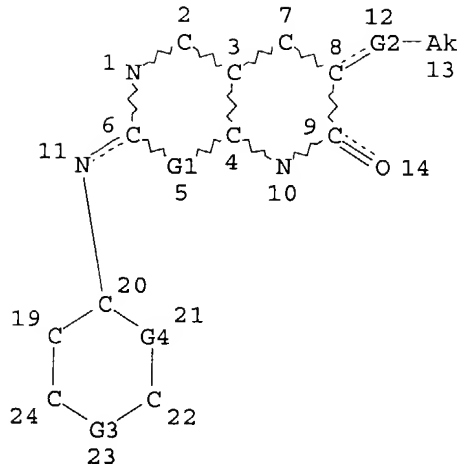

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Ak—Cb
17 18

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DEFAULT ECLEVEL IS LIMITED

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FILE COVERS 1907 - 4 Aug 2004 VOL 141 ISS 6
FILE LAST UPDATED: 3 Aug 2004 (20040803/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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L40 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:591180 HCAPLUS
DN 139:149646
TI Preparation of pyrido[2,3-d]pyrimidin-7-ones as cdk4 inhibitors
IN Barvian, Mark Robert; Booth, Richard John; Quin, John, III; Repine, Joseph Thomas; Sheehan, Derek James; Toogood, Peter Laurence; Vanderwel, Scott Norman; Zhou, Hairong
PA Warner-Lambert Company Llc, USA
SO PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003062236	A1	20030731	WO 2003-IB59	20030110
	WO 2003062236	C1	20031224		
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	US 2003149001	A1	20030807	US 2003-345778	20030116
PRAI	US 2002-350877P	P	20020122		

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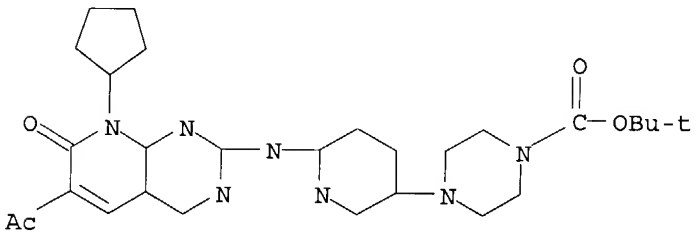
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein X1, X2, X3 = independently H, halo, alkyl, (un)substituted amino, acyl, carbamoyl, sulfamoyl, etc.; R1 = independently H, halo, alkyl, haloalkyl, hydroxyalkyl, cycloalkyl; R2, R4 = independently H, halo, (un)substituted alkyl, amino, acyl, sulfamoyl, carbamoyl, etc.; R3 = H, aryl, alkyl, alkoxy, cycloalkyl, heterocyclyl; R1CCR2 = 3-7 carbocyclic or heterocyclic ring; and their pharmaceutically acceptable salts, esters, amides, or prodrugs] were prepared as cyclin-dependent kinases 4 (cdk4) inhibitors. Examples include 135 invention compds., three biol. assays, one tablet formulation, and a parenteral solution For example, compound II.cntdot.2.2HCl was prepared by the solventless reaction of 6-bromo-8-cyclopentyl-2-methylsulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one with 4-(6-aminopyridin-3-yl)piperazine-1-carboxylic acid tert-Bu ester at 1200C for 1 h, followed by deprotection in the presence of gaseous HCl. II selectively inhibited cdk4 over cdk2 with IC50 values of 0.016 .mu.M and 6.052 .mu.M, resp. Thus, I and their formulations are useful for treating cell proliferative disorders, such as cancer, atherosclerosis, and restenosis (no data).

IT **571189-08-7P**, 4-[6-[(6-Acetyl-8-cyclopentyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl)amino]pyridin-3-yl]piperazine-1-carboxylic acid tert-butyl ester
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(cdk4 inhibitor; preparation of pyrido[2,3-d]pyrimidinones as cdk4 inhibitors for treating cell proliferative disorders)

RN 571189-08-7 HCAPLUS

CN 1-Piperazinecarboxylic acid, 4-[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

IT **571189-08-7P**, 4-[6-[(6-Acetyl-8-cyclopentyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl)amino]pyridin-3-yl]piperazine-1-carboxylic acid tert-butyl ester **571189-28-1P**, 4-[6-[[8-Cyclopentyl-6-(2-ethoxyethoxy)-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl]amino]pyridin-3-yl]-piperazine-1-carboxylic acid tert-butyl ester **571189-57-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(cdk4 inhibitor; preparation of pyrido[2,3-d]pyrimidinones as cdk4 inhibitors for treating cell proliferative disorders)

IT **571188-90-4P**, 4-[6-[(8-Cyclopentyl-6-isobutoxy-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl)amino]pyridin-3-yl]piperazine-1-carboxylic acid tert-butyl ester **571188-91-5P**, 8-Cyclopentyl-6-isobutoxy-2-[(5-piperazin-1-ylpyridin-2-yl)amino]-8H-

pyrido[2,3-d]pyrimidin-7-one dihydrochloride **571189-09-8P** **571189-11-2P** **571189-31-6P** **571189-34-9P**, 6-Acetyl-2-[5-[bis(2-methoxyethyl)amino]pyridin-2-ylamino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571189-51-0P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[[5-(4-methylpiperazin-1-yl)pyridin-2-yl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **571189-54-3P**, 6-Acetyl-2-[[5-(3-aminopyrrolidin-1-yl)pyridin-2-yl]amino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571189-62-3P** **571189-63-4P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-(pyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **571189-72-5P** **571189-77-0P** **571189-81-6P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[(5-morpholin-4-ylpyridin-2-yl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **571189-84-9P** **571190-11-9P**, 6-Acetyl-8-cyclopentyl-2-[5-(2,6-dimethylmorpholin-4-yl)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571190-17-5P**, 6-Acetyl-8-cyclopentyl-2-[[5-(3,5-dimethylpiperazin-1-yl)pyridin-2-yl]amino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571190-18-6P**, 6-Acetyl-8-cyclopentyl-2-[[5-(3,3-dimethylpiperazin-1-yl)pyridin-2-yl]amino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571190-20-0P** **571190-28-8P**, 8-Cyclopentyl-5-methyl-2-[(5-piperazin-1-ylpyridin-2-yl)amino]-6-propionyl-8H-pyrido[2,3-d]pyrimidin-7-one **571190-29-9P**, 6-Acetyl-8-cyclopentyl-2-[[5-(piperazin-1-yl)pyridin-2-yl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **571190-30-2P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[[5-(piperazin-1-yl)pyridin-2-yl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **571190-41-5P**, 6-Acetyl-8-cyclopentyl-2-[5-(3-ethylaminopyrrolidin-1-yl)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571190-42-6P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[(5-pyrrolidin-1-ylpyridin-2-yl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **571190-43-7P**, 6-Acetyl-2-[5-[3-(1-amino-1-methylethyl)pyrrolidin-1-yl]pyridin-2-ylamino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571190-44-8P**, 1-[6-(6-Acetyl-8-cyclopentyl-5-methyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-ylamino)pyridin-3-yl]pyrrolidine-2-carboxylic acid **571190-45-9P**, 6-Acetyl-8-cyclopentyl-2-[5-(4-diethylaminobutylamino)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-13-4P**, 6-Acetyl-8-cyclopentyl-2-(5-diethylaminopyridin-2-ylamino)-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-14-5P**, 6-Acetyl-2-[5-[bis(2-hydroxyethyl)amino]pyridin-2-ylamino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-15-6P**, 6-Acetyl-2-[5-(2-aminoethylamino)pyridin-2-ylamino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-16-7P**, 6-Acetyl-8-cyclopentyl-2-(5-dimethylaminopyridin-2-ylamino)-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-17-8P**, N-[6-(6-Acetyl-8-cyclopentyl-5-methyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-ylamino)pyridin-3-yl]-N-methylacetamide **571191-18-9P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-methoxyethoxy)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-19-0P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-methoxyethoxymethyl)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-20-3P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-diethylaminoethoxy)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-21-4P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[6-methyl-5-(piperazin-1-yl)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-22-5P** **571191-23-6P**, 6-Acetyl-8-cyclopentyl-2-[5-(morpholin-4-yl)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-24-7P**, 6-Acetyl-8-cyclopentyl-2-(5-diethylaminopyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **571191-25-8P**, 6-Acetyl-2-[5-[bis(2-hydroxyethyl)amino]pyridin-2-ylamino]-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-26-9P**, 6-Acetyl-2-[5-[bis(2-methoxyethyl)amino]pyridin-2-ylamino]-8-cyclopentyl-8H-pyrido[2,3-

d]pyrimidin-7-one **571191-27-0P**, 6-Acetyl-2-[5-(2-aminoethylamino)pyridin-2-ylamino]-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-28-1P**, 6-Acetyl-8-cyclopentyl-2-(5-dimethylaminopyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **571191-29-2P**, N-[6-(6-Acetyl-8-cyclopentyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-ylamino)pyridin-3-yl]-N-methylacetamide **571191-30-5P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-methoxyethoxy)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-31-6P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-methoxyethoxymethyl)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-32-7P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-diethylaminoethoxy)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-33-8P**, 6-Acetyl-8-cyclopentyl-2-[(5-pyrrolidin-1-ylpyridin-2-yl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-34-9P**, 6-Acetyl-8-cyclopentyl-2-[6-methyl-5-(piperazin-1-yl)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-54-3P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-methoxyethylamino)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-55-4P**, 6-Acetyl-2-[(5-azetidin-1-ylpyridin-2-yl)amino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-56-5P**, 6-Acetyl-2-[(5-azepan-1-ylpyridin-2-yl)amino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-57-6P**, N-[6-(6-Acetyl-8-cyclopentyl-5-methyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-ylamino)pyridin-3-yl]acetamide **571191-58-7P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-(5-phenylaminopyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **571191-59-8P**, 6-Acetyl-8-cyclopentyl-2-[5-(4-fluorobenzylamino)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-60-1P**, N-[6-(6-Acetyl-8-cyclopentyl-5-methyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-ylamino)pyridin-3-yl]methanesulfonamide **571191-61-2P**, 6-Acetyl-8-cyclopentyl-2-[5-(methylsulfonyl)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-62-3P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-(5-phenylpyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **571192-12-6P 571192-13-7P 571192-14-8P**, 6-Acetyl-2-[5-(3-aminopyrrolidine-1-carbonyl)pyridin-2-ylamino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571192-15-9P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[5-(morpholine-4-carbonyl)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571192-32-0P 571192-33-1P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[5-(morpholine-4-sulfonyl)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571192-34-2P**, 6-Acetyl-2-[5-(3-aminopyrrolidine-1-sulfonyl)pyridin-2-ylamino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571192-35-3P 571192-36-4P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-([1,6]naphthyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **571192-37-5P 571192-39-7P**, 6-Acetyl-2-[(3-chloro-5-(piperazin-1-yl)pyridin-2-yl)amino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571192-40-0P**, 4-[6-Acetyl-5-methyl-7-oxo-2-(pyridin-2-ylamino)-7H-pyrido[2,3-d]pyrimidin-8-yl]cyclohexanecarboxylic acid **571192-41-1P**, 4-[6-Acetyl-2-(5-dimethylaminopyridin-2-ylamino)-5-methyl-7-oxo-7H-pyrido[2,3-d]pyrimidin-8-yl]cyclohexanecarboxylic acid **571192-51-3P**, 6-Acetyl-5-methyl-2-(5-methylpyridin-2-ylamino)-8-piperidin-4-yl-8H-pyrido[2,3-d]pyrimidin-7-one **571192-52-4P**, 6-Acetyl-2-[5-(3,4-dihydroxypyrrolidin-1-yl)pyridin-2-ylamino]-8-methoxymethyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cdk4 inhibitor; preparation of pyrido[2,3-d]pyrimidinones as cdk4 inhibitors for treating cell proliferative disorders)

IT **571189-64-5P**, 6-Acetyl-2-amino-8-cyclopentyl-5-methyl-8H-

pyrido[2,3-d]pyrimidin-7-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrido[2,3-d]pyrimidinones as cdk4 inhibitors for treating cell proliferative disorders)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d bib abs hitstr l41

L41 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:591180 HCAPLUS
DN 139:149646
TI Preparation of pyrido[2,3-d]pyrimidin-7-ones as cdk4 inhibitors
IN Barvian, Mark Robert; Booth, Richard John; Quin, John, III; Repine, Joseph Thomas; Sheehan, Derek James; Toogood, Peter Laurence; Vanderwel, Scott Norman; Zhou, Hairong
PA Warner-Lambert Company Llc, USA
SO PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PRAI	US 2002-350877P	P	20020122 <--		

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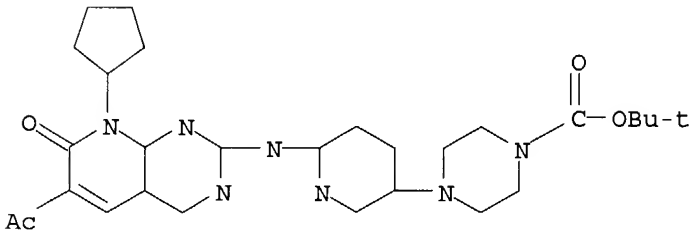
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein X1, X2, X3 = independently H, halo, alkyl, (un)substituted amino, acyl, carbamoyl, sulfamoyl, etc.; R1 = independently H, halo, alkyl, haloalkyl, hydroxyalkyl, cycloalkyl; R2, R4 = independently H, halo, (un)substituted alkyl, amino, acyl, sulfamoyl, carbamoyl, etc.; R3 = H, aryl, alkyl, alkoxy, cycloalkyl, heterocyclyl; R1CCR2 = 3-7 carbocyclic or heterocyclic ring; and their pharmaceutically acceptable salts, esters, amides, or prodrugs] were prepared as cyclin-dependent kinases 4 (cdk4) inhibitors. Examples include 135 invention compds., three biol. assays, one tablet formulation, and a parenteral solution For example, compound II.cntdot.2.2HCl was prepared by the solventless reaction of 6-bromo-8-cyclopentyl-2-methylsulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one with 4-(6-aminopyridin-3-yl)piperazine-1-carboxylic acid tert-Bu ester at 1200C for 1 h, followed by deprotection

in the presence of gaseous HCl. II selectively inhibited cdk4 over cdk2 with IC50 values of 0.016 .mu.M and 6.052 .mu.M, resp. Thus, I and their formulations are useful for treating cell proliferative disorders, such as cancer, atherosclerosis, and restenosis (no data).

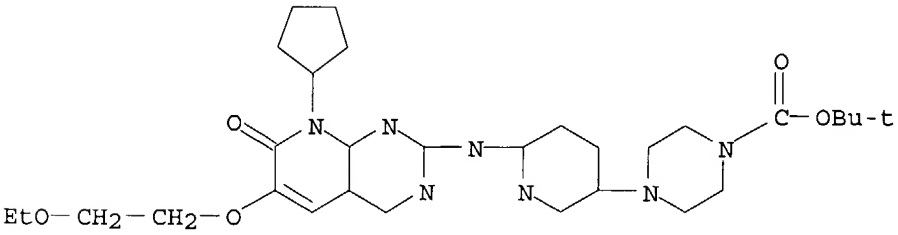
IT **571189-08-7P**, 4-[6-[(6-Acetyl-8-cyclopentyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl)amino]pyridin-3-yl]piperazine-1-carboxylic acid tert-butyl ester **571189-28-1P**, 4-[6-[[8-Cyclopentyl-6-(2-ethoxyethoxy)-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl]amino]pyridin-3-yl]-piperazine-1-carboxylic acid tert-butyl ester **571189-57-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(cdk4 inhibitor; preparation of pyrido[2,3-d]pyrimidinones as cdk4 inhibitors for treating cell proliferative disorders)

RN 571189-08-7 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



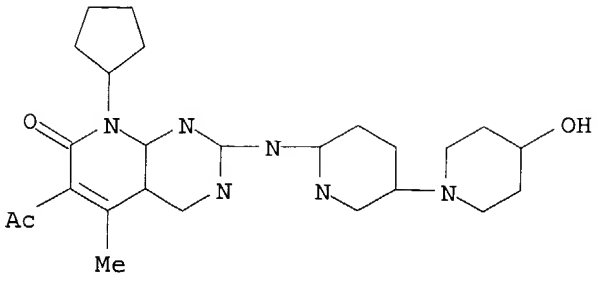
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 571189-28-1 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[6-[[8-cyclopentyl-6-(2-ethoxyethoxy)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]-3-pyridinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 571189-57-6 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(4-hydroxy-1-piperidinyl)-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



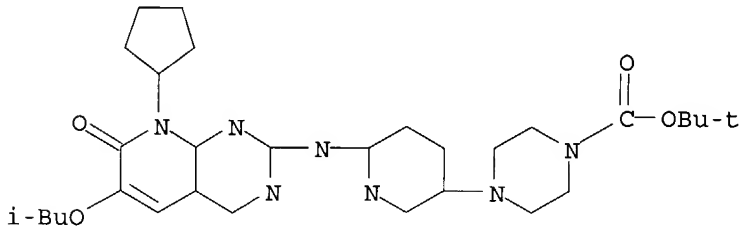
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

IT **571188-90-4P**, 4-[6-[(8-Cyclopentyl-6-isobutoxy-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl)amino]pyridin-3-yl]piperazine-1-carboxylic acid tert-butyl ester **571188-91-5P**, 8-Cyclopentyl-6-isobutoxy-2-[(5-piperazin-1-ylpyridin-2-yl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one dihydrochloride **571189-09-8P** **571189-11-2P** **571189-31-6P** **571189-34-9P**, 6-Acetyl-2-[5-[bis(2-methoxyethyl)amino]pyridin-2-ylamino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571189-51-0P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[[5-(4-methylpiperazin-1-yl)pyridin-2-yl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **571189-54-3P**, 6-Acetyl-2-[[5-(3-aminopyrrolidin-1-yl)pyridin-2-yl]amino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571189-62-3P** **571189-63-4P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-(pyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **571189-72-5P** **571189-77-0P** **571189-81-6P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[(5-morpholin-4-ylpyridin-2-yl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **571189-84-9P** **571190-11-9P**, 6-Acetyl-8-cyclopentyl-2-[5-(2,6-dimethylmorpholin-4-yl)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571190-17-5P**, 6-Acetyl-8-cyclopentyl-2-[[5-(3,5-dimethylpiperazin-1-yl)pyridin-2-yl]amino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571190-18-6P**, 6-Acetyl-8-cyclopentyl-2-[[5-(3,3-dimethylpiperazin-1-yl)pyridin-2-yl]amino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571190-20-0P** **571190-28-8P**, 8-Cyclopentyl-5-methyl-2-[(5-piperazin-1-ylpyridin-2-yl)amino]-6-propionyl-8H-pyrido[2,3-d]pyrimidin-7-one **571190-29-9P**, 6-Acetyl-8-cyclopentyl-2-[[5-(piperazin-1-yl)pyridin-2-yl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **571190-30-2P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[[5-(piperazin-1-yl)pyridin-2-yl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **571190-41-5P**, 6-Acetyl-8-cyclopentyl-2-[5-(3-ethylaminopyrrolidin-1-yl)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571190-42-6P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[(5-pyrrolidin-1-ylpyridin-2-yl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **571190-43-7P**, 6-Acetyl-2-[5-[3-(1-amino-1-methylethyl)pyrrolidin-1-yl]pyridin-2-ylamino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571190-44-8P**, 1-[6-(6-Acetyl-8-cyclopentyl-5-methyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-ylamino)pyridin-3-yl]pyrrolidine-2-carboxylic acid **571190-45-9P**, 6-Acetyl-8-cyclopentyl-2-[5-(4-diethylaminobutylamino)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-13-4P**, 6-Acetyl-8-cyclopentyl-2-(5-diethylaminopyridin-2-ylamino)-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-14-5P**, 6-Acetyl-2-[5-[bis(2-hydroxyethyl)amino]pyridin-2-ylamino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-15-6P**, 6-Acetyl-2-[5-(2-aminoethylamino)pyridin-2-ylamino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-16-7P**, 6-Acetyl-8-cyclopentyl-2-(5-dimethylaminopyridin-2-

ylamino)-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-17-8P**, N-[6-(6-Acetyl-8-cyclopentyl-5-methyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-ylamino)pyridin-3-yl]-N-methylacetamide **571191-18-9P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-methoxyethoxy)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-19-0P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-methoxyethoxymethyl)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-20-3P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-diethylaminoethoxy)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-21-4P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[6-methyl-5-(piperazin-1-yl)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-22-5P** **571191-23-6P**, 6-Acetyl-8-cyclopentyl-2-[5-(morpholin-4-yl)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-24-7P**, 6-Acetyl-8-cyclopentyl-2-(5-diethylaminopyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **571191-25-8P**, 6-Acetyl-2-[5-[bis(2-hydroxyethyl)amino]pyridin-2-ylamino]-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-26-9P**, 6-Acetyl-2-[5-[bis(2-methoxyethyl)amino]pyridin-2-ylamino]-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-27-0P**, 6-Acetyl-2-[5-(2-aminoethylamino)pyridin-2-ylamino]-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-28-1P**, 6-Acetyl-8-cyclopentyl-2-(5-dimethylaminopyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **571191-29-2P**, N-[6-(6-Acetyl-8-cyclopentyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-ylamino)pyridin-3-yl]-N-methylacetamide **571191-30-5P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-methoxyethoxy)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-31-6P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-methoxyethoxymethyl)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-32-7P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-diethylaminoethoxy)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-33-8P**, 6-Acetyl-8-cyclopentyl-2-[(5-pyrrolidin-1-ylpyridin-2-yl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-34-9P**, 6-Acetyl-8-cyclopentyl-2-[6-methyl-5-(piperazin-1-yl)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571191-54-3P**, 6-Acetyl-8-cyclopentyl-2-[5-(2-methoxyethylamino)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-55-4P**, 6-Acetyl-2-[(5-azetidin-1-ylpyridin-2-yl)amino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-56-5P**, 6-Acetyl-2-[(5-azepan-1-ylpyridin-2-yl)amino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-57-6P**, N-[6-(6-Acetyl-8-cyclopentyl-5-methyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-ylamino)pyridin-3-yl]acetamide **571191-58-7P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-(5-phenylaminopyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **571191-59-8P**, 6-Acetyl-8-cyclopentyl-2-[5-(4-fluorobenzylamino)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-60-1P**, N-[6-(6-Acetyl-8-cyclopentyl-5-methyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-ylamino)pyridin-3-yl]methanesulfonamide **571191-61-2P**, 6-Acetyl-8-cyclopentyl-2-[5-(methylsulfonyl)pyridin-2-ylamino]-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571191-62-3P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-(5-phenylpyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **571192-12-6P** **571192-13-7P** **571192-14-8P**, 6-Acetyl-2-[5-(3-aminopyrrolidine-1-carbonyl)pyridin-2-ylamino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571192-15-9P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[5-(morpholine-4-carbonyl)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571192-32-0P** **571192-33-1P**, 6-Acetyl-8-cyclopentyl-5-methyl-2-[5-(morpholine-4-sulfonyl)pyridin-2-ylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **571192-34-2P**, 6-Acetyl-2-[5-(3-aminopyrrolidine-1-sulfonyl)pyridin-2-ylamino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571192-35-3P** **571192-36-4P**, 6-Acetyl-8-cyclopentyl-5-

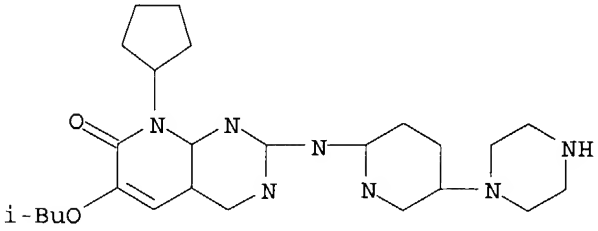
methyl-2-([1,6]naphthyridin-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **571192-37-5P 571192-39-7P**, 6-Acetyl-2-[(3-chloro-5-(piperazin-1-yl)pyridin-2-yl)amino]-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one **571192-40-0P**, 4-[6-Acetyl-5-methyl-7-oxo-2-(pyridin-2-ylamino)-7H-pyrido[2,3-d]pyrimidin-8-yl]cyclohexanecarboxylic acid **571192-41-1P**, 4-[6-Acetyl-2-(5-dimethylaminopyridin-2-ylamino)-5-methyl-7-oxo-7H-pyrido[2,3-d]pyrimidin-8-yl]cyclohexanecarboxylic acid **571192-51-3P**, 6-Acetyl-5-methyl-2-(5-methylpyridin-2-ylamino)-8-piperidin-4-yl-8H-pyrido[2,3-d]pyrimidin-7-one **571192-52-4P**, 6-Acetyl-2-[5-(3,4-dihydroxypyrrolidin-1-yl)pyridin-2-ylamino]-8-methoxymethyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cdk4 inhibitor; preparation of pyrido[2,3-d]pyrimidinones as cdk4 inhibitors for treating cell proliferative disorders)

RN 571188-90-4 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[6-[[8-cyclopentyl-7,8-dihydro-6-(2-methylpropoxy)-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]-3-pyridinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

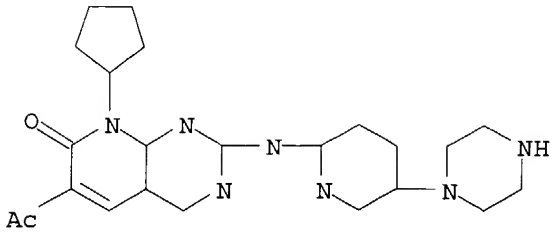
RN 571188-91-5 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-cyclopentyl-6-(2-methylpropoxy)-2-[[5-(1-piperazinyl)-2-pyridinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

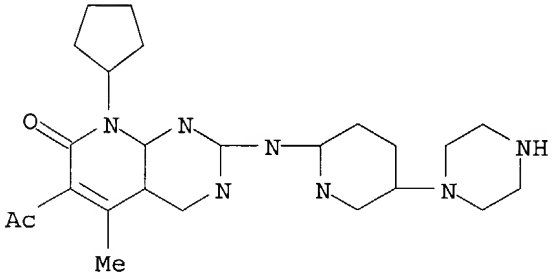
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 571189-09-8 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(1-piperazinyl)-2-pyridinyl]amino]-, hydrochloride (4:17) (9CI) (CA INDEX NAME)



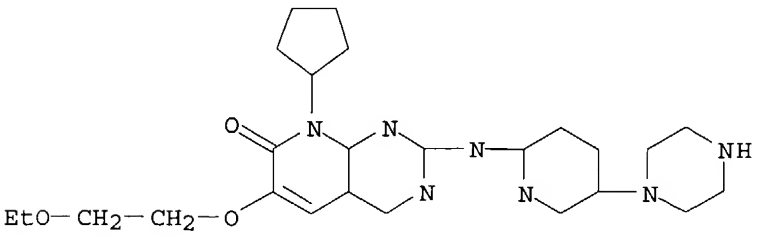
●17/4 HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571189-11-2 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-5-methyl-2-[[5-(1-piperazinyl)-2-pyridinyl]amino]-, hydrochloride (20:37) (9CI) (CA INDEX NAME)



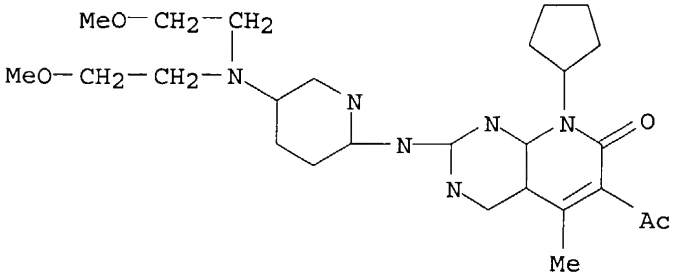
●37/20 HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571189-31-6 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-cyclopentyl-6-(2-ethoxyethoxy)-2-[[5-(1-piperazinyl)-2-pyridinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

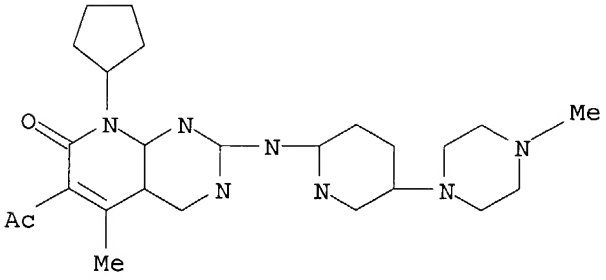


●2 HCl

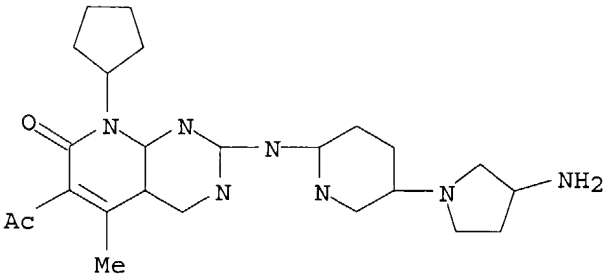
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571189-34-9 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-2-[[5-[bis(2-methoxyethyl)amino]-2-pyridinyl]amino]-8-cyclopentyl-5-methyl- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571189-51-0 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-5-methyl-2-[[5-(4-methyl-1-piperazinyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)

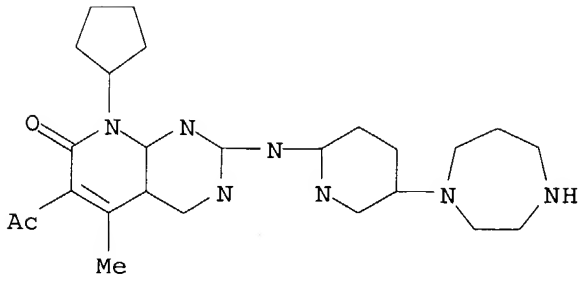


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571189-54-3 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-2-[[5-(3-amino-1-pyrrolidinyl)-2-pyridinyl]amino]-8-cyclopentyl-5-methyl- (9CI) (CA INDEX NAME)



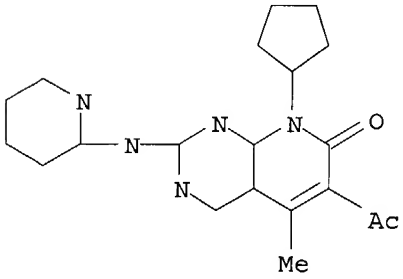
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571189-62-3 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(hexahydro-1H-1,4-diazepin-1-yl)-2-pyridinyl]amino]-5-methyl-, hydrochloride (5:14)

(9CI) (CA INDEX NAME)

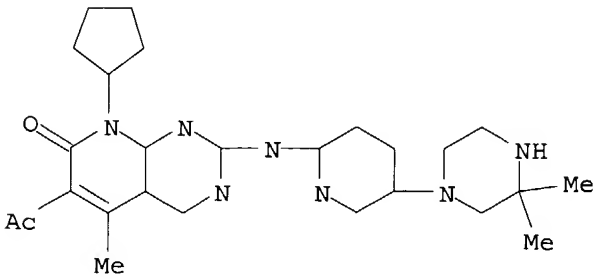


●14/5 HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571189-63-4 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-5-methyl-2-(2-pyridinylamino)- (9CI) (CA INDEX NAME)

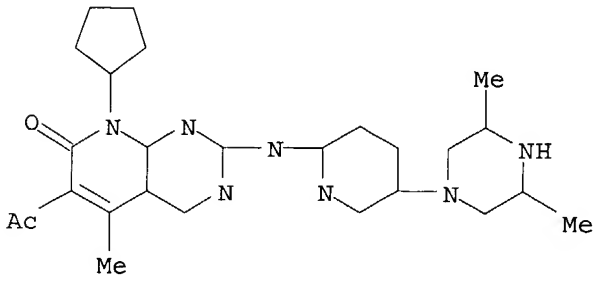


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571189-72-5 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(3,3-dimethyl-1-piperazinyl)-2-pyridinyl]amino]-5-methyl-, hydrochloride (9CI) (CA INDEX NAME)



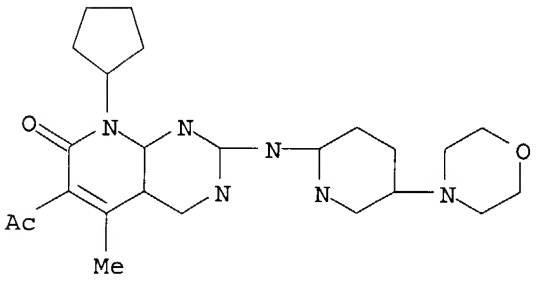
●x HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571189-77-0 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(3,5-dimethyl-1-piperazinyl)-2-pyridinyl]amino]-5-methyl-, hydrochloride (10:27) (9CI) (CA INDEX NAME)

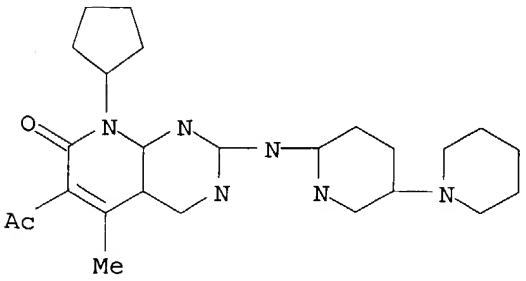


●27/10 HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571189-81-6 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-5-methyl-2-[[5-(4-morpholinyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)

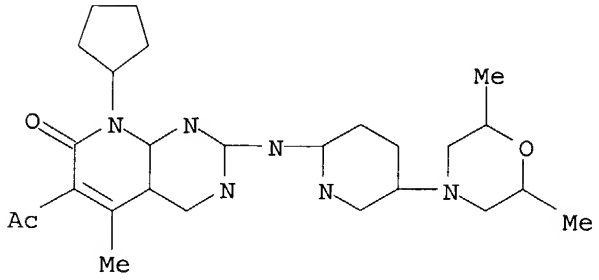


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571189-84-9 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-5-methyl-2-[[5-(1-piperidinyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)

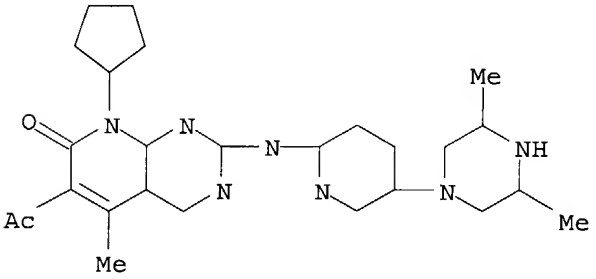


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

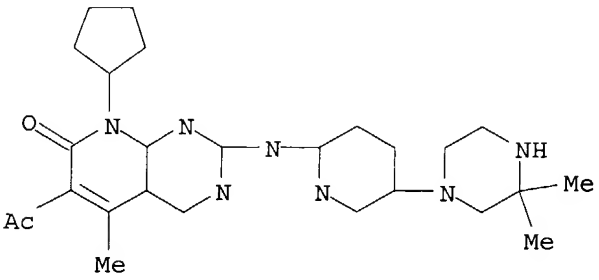
RN 571190-11-9 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(2,6-dimethyl-4-morpholinyl)-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



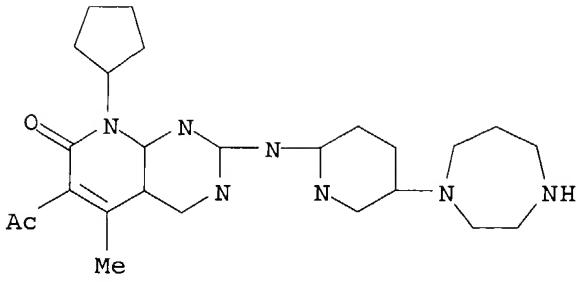
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571190-17-5 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(3,5-dimethyl-1-piperazinyl)-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



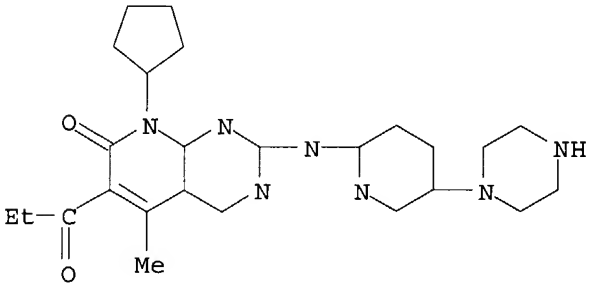
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571190-18-6 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(3,3-dimethyl-1-piperazinyl)-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



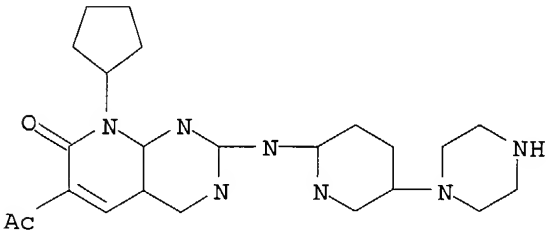
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571190-20-0 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(hexahydro-1H-1,4-diazepin-1-yl)-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



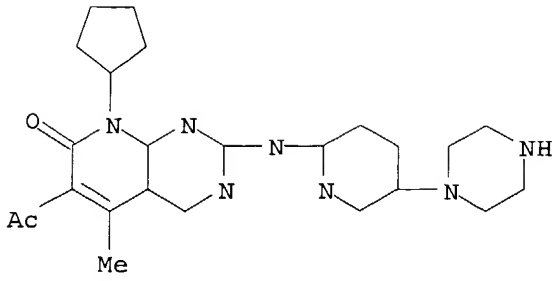
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571190-28-8 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-cyclopentyl-5-methyl-6-(1-oxopropyl)-2-[[5-(1-piperazinyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



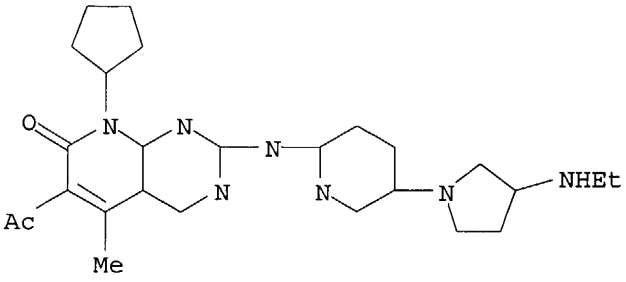
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571190-29-9 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(1-piperazinyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



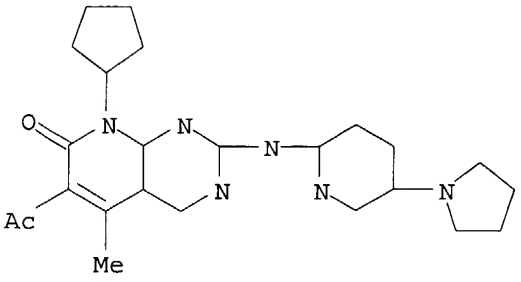
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571190-30-2 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-5-methyl-2-[[5-(1-piperazinyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



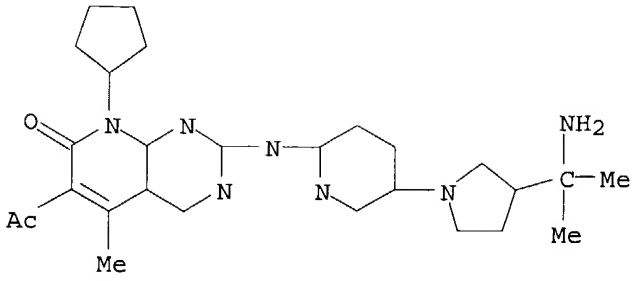
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571190-41-5 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-[3-(ethylamino)-1-pyrrolidinyl]-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571190-42-6 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-5-methyl-2-[[5-(1-pyrrolidinyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)

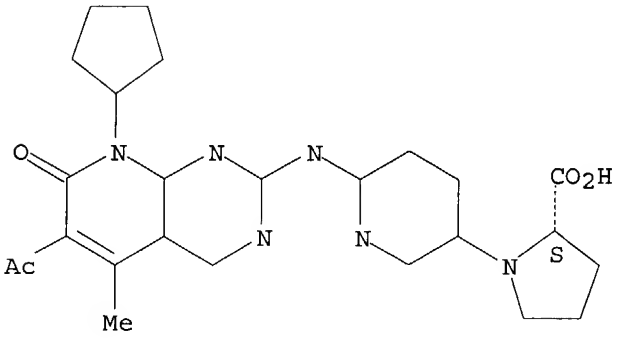


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571190-43-7 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-2-[[5-[3-(1-amino-1-methylethyl)-1-pyrrolidinyl]-2-pyridinyl]amino]-8-cyclopentyl-5-methyl- (9CI) (CA INDEX NAME)

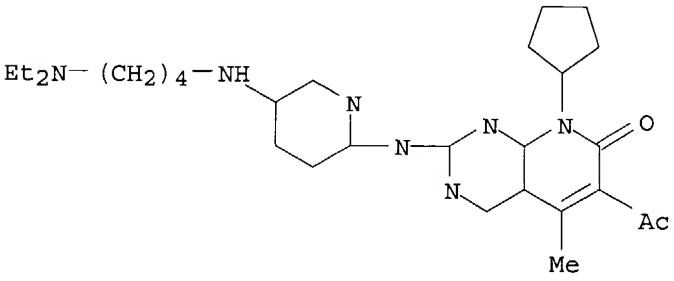


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571190-44-8 HCAPLUS
CN L-Proline, 1-[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-5-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]- (9CI) (CA INDEX NAME)

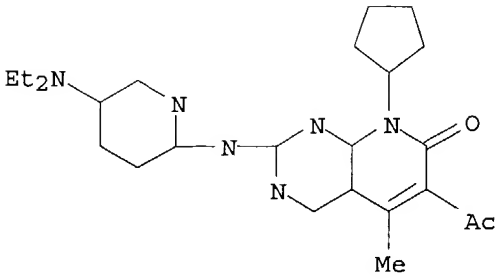
Absolute stereochemistry.



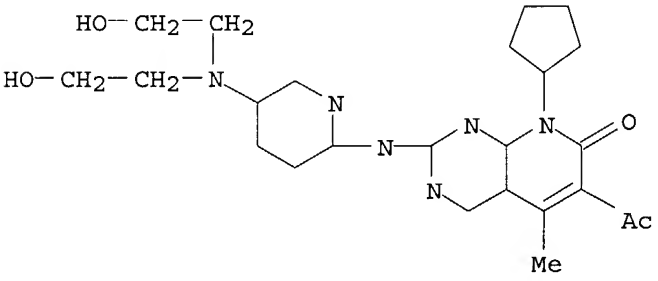
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571190-45-9 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-[[4-(diethylamino)butyl]amino]-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



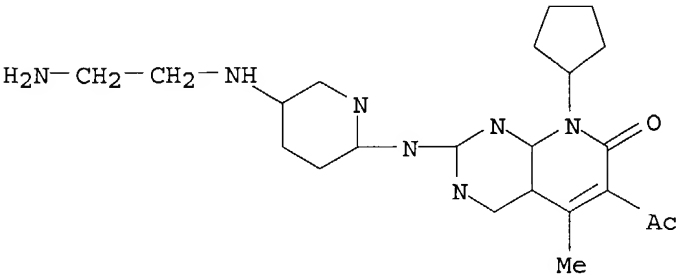
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-13-4 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(diethylamino)-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



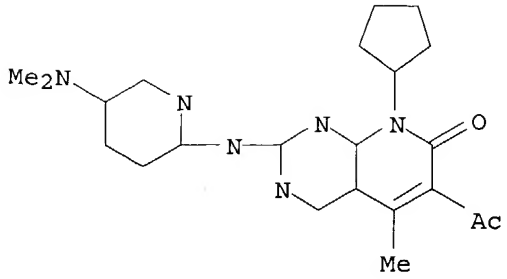
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-14-5 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-2-[[5-[bis(2-hydroxyethyl)amino]-2-pyridinyl]amino]-8-cyclopentyl-5-methyl- (9CI) (CA INDEX NAME)



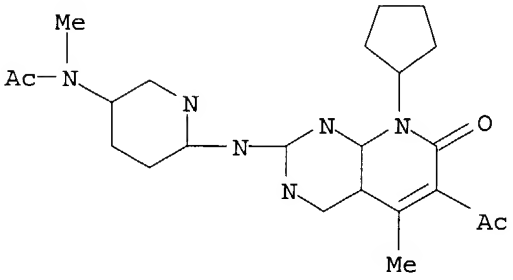
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-15-6 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-2-[[5-[(2-aminoethyl)amino]-2-pyridinyl]amino]-8-cyclopentyl-5-methyl- (9CI) (CA INDEX NAME)



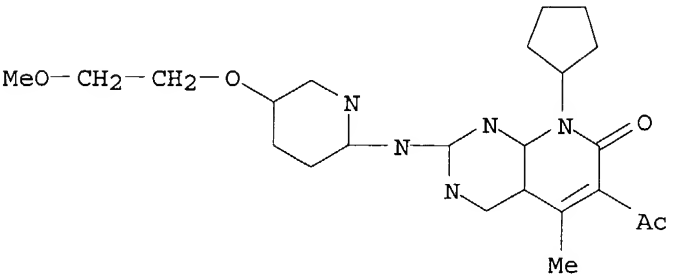
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-16-7 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(dimethylamino)-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



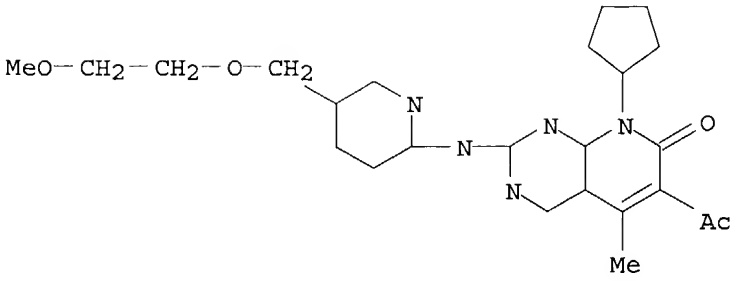
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-17-8 HCAPLUS
CN Acetamide, N-[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-5-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]-N-methyl- (9CI) (CA INDEX NAME)



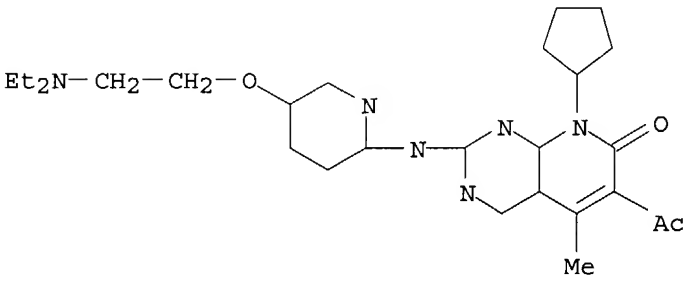
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-18-9 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(2-methoxyethoxy)-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



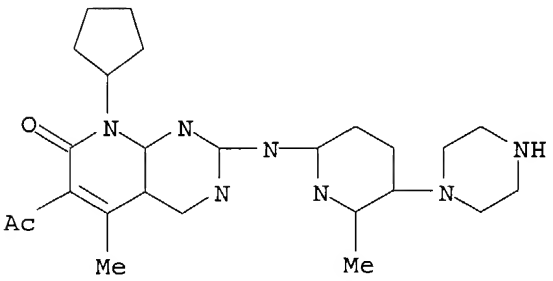
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-19-0 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-[(2-methoxyethoxy)methyl]-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



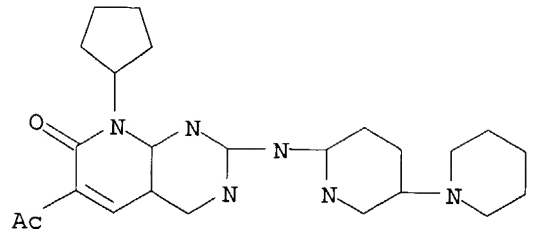
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-20-3 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-[2-(diethylamino)ethoxy]-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



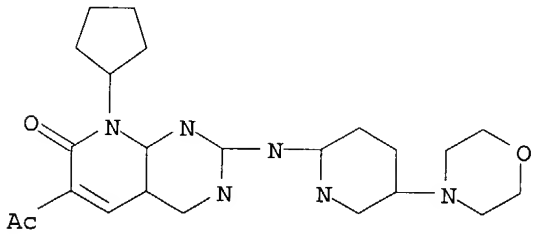
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-21-4 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-5-methyl-2-[[6-methyl-5-(1-piperazinyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



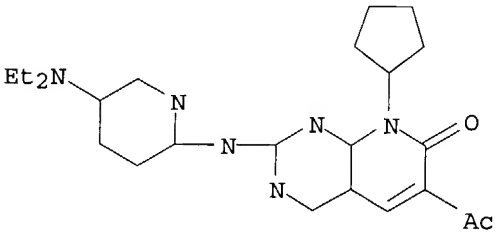
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-22-5 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(1-piperidinyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



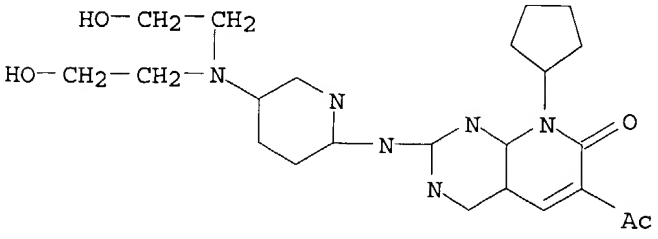
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-23-6 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(4-morpholinyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-24-7 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(diethylamino)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)

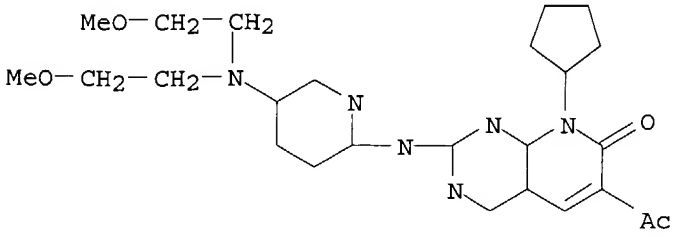


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-25-8 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-2-[[5-[bis(2-hydroxyethyl)amino]-2-pyridinyl]amino]-8-cyclopentyl- (9CI) (CA INDEX NAME)

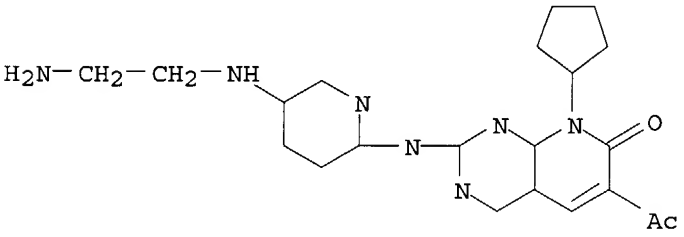


Searched by Noble Jarrell

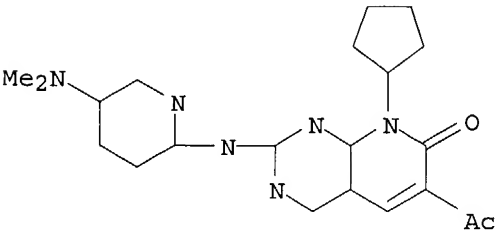
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-26-9 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-2-[[5-[bis(2-methoxyethyl)amino]-2-pyridinyl]amino]-8-cyclopentyl- (9CI) (CA INDEX NAME)



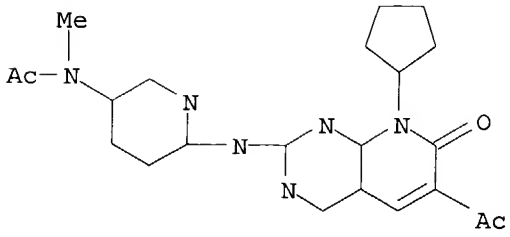
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-27-0 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-2-[[5-[(2-aminoethyl)amino]-2-pyridinyl]amino]-8-cyclopentyl- (9CI) (CA INDEX NAME)



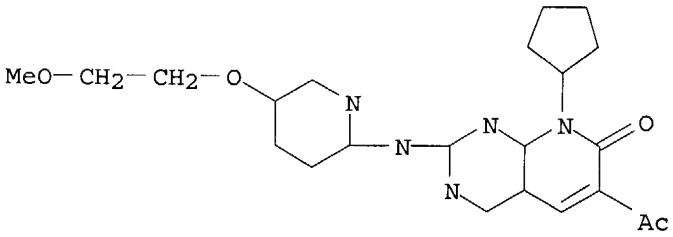
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-28-1 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(dimethylamino)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



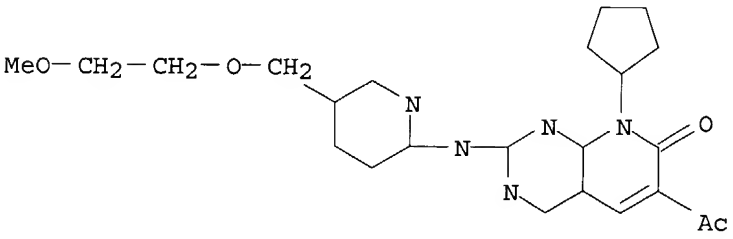
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-29-2 HCAPLUS
CN Acetamide, N-[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]-N-methyl- (9CI) (CA INDEX NAME)



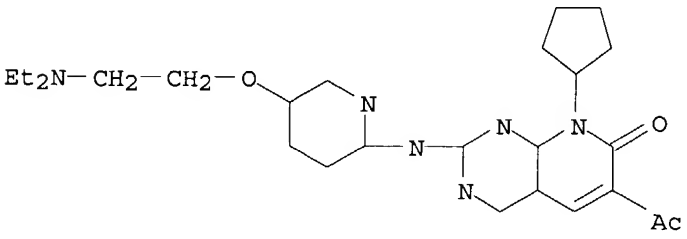
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-30-5 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(2-methoxyethoxy)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-31-6 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-[(2-methoxyethoxy)methyl]-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



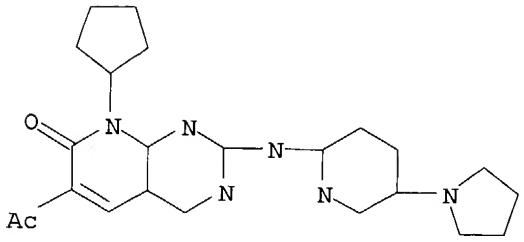
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-32-7 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-[2-(diethylamino)ethoxy]-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



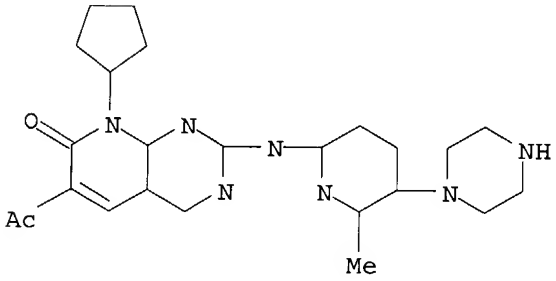
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

Searched by Noble Jarrell

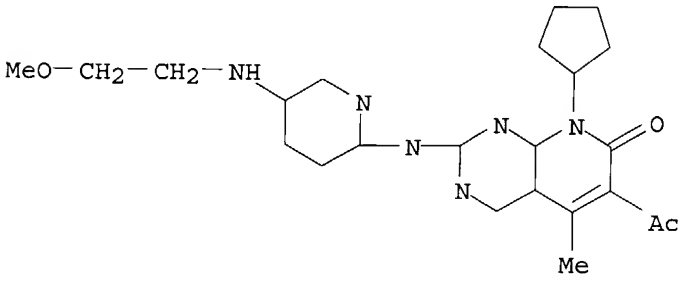
RN 571191-33-8 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(1-pyrrolidinyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



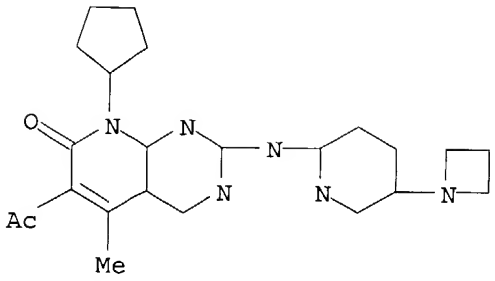
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-34-9 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[6-methyl-5-(1-piperazinyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



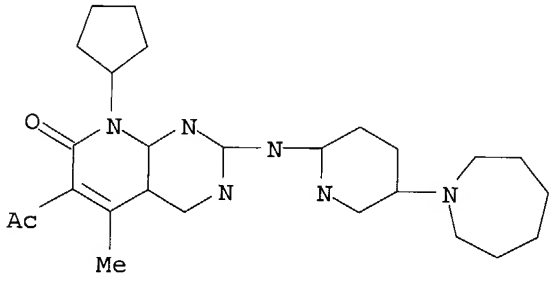
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-54-3 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-[(2-methoxyethyl)amino]-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



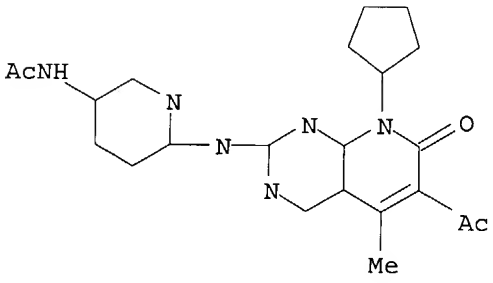
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-55-4 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-2-[[5-(1-azetidinyl)-2-pyridinyl]amino]-8-cyclopentyl-5-methyl- (9CI) (CA INDEX NAME)



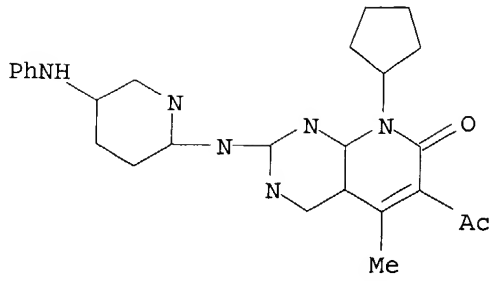
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-56-5 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(hexahydro-1H-azepin-1-yl)-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



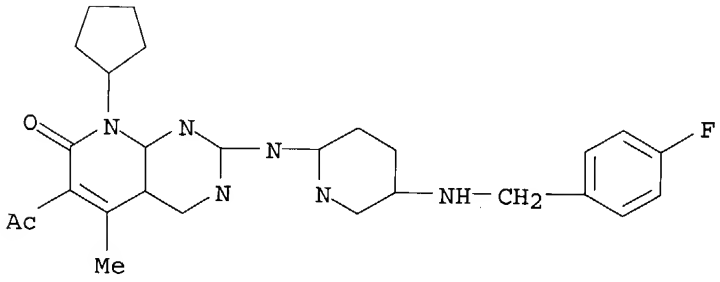
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-57-6 HCAPLUS
CN Acetamide, N-[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-5-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]- (9CI) (CA INDEX NAME)



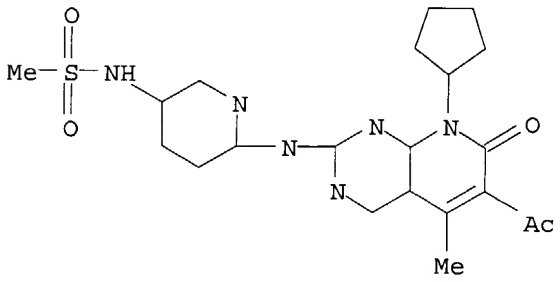
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-58-7 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-5-methyl-2-[[5-(phenylamino)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



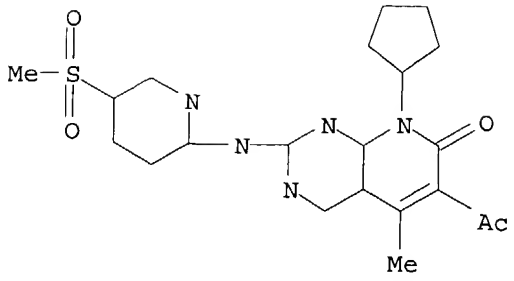
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-59-8 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-[[(4-fluorophenyl)methyl]amino]-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



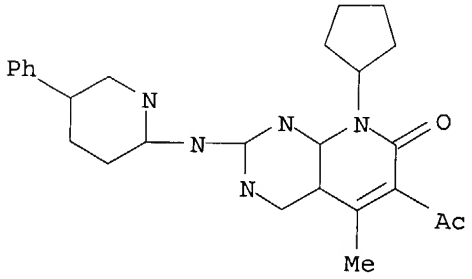
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-60-1 HCAPLUS
CN Methanesulfonamide, N-[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-5-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]- (9CI) (CA INDEX NAME)



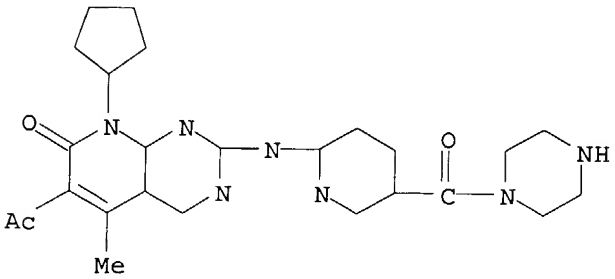
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-61-2 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-5-methyl-2-[[5-(methylsulfonyl)-2-pyridinyl]amino]- (9CI) (CA INDEX NAME)



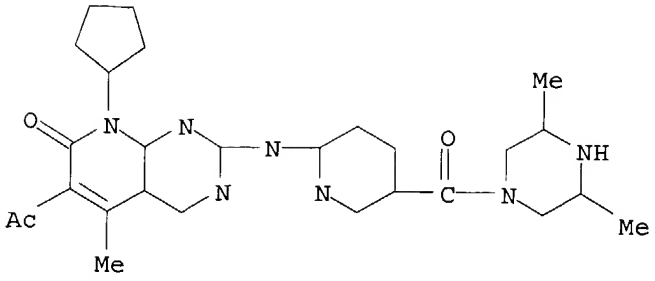
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571191-62-3 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-5-methyl-2-[(5-phenyl-2-pyridinyl)amino]- (9CI) (CA INDEX NAME)



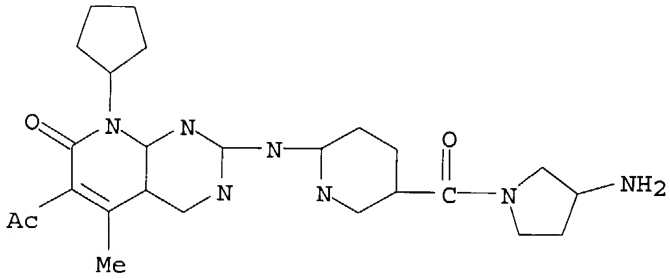
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-12-6 HCAPLUS
CN Piperazine, 1-[[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-5-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]carbonyl]- (9CI) (CA INDEX NAME)



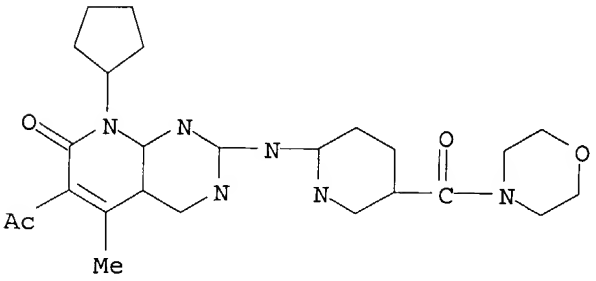
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-13-7 HCAPLUS
CN Piperazine, 1-[[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-5-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]carbonyl]-3,5-dimethyl- (9CI) (CA INDEX NAME)



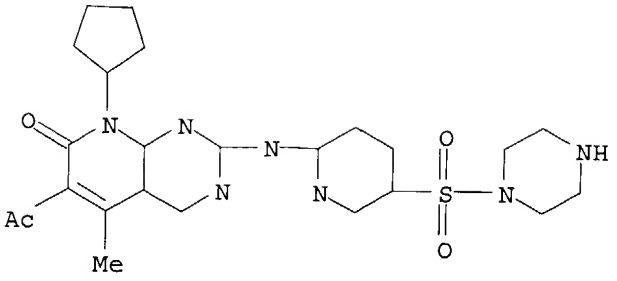
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-14-8 HCAPLUS
CN Pyrrolidine, 1-[[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-5-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]carbonyl]-3-amino- (9CI) (CA INDEX NAME)



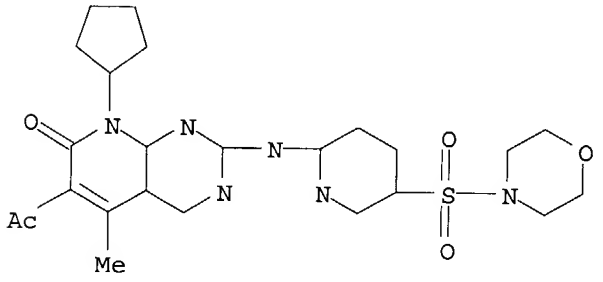
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-15-9 HCAPLUS
CN Morpholine, 4-[[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-5-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]carbonyl]- (9CI) (CA INDEX NAME)



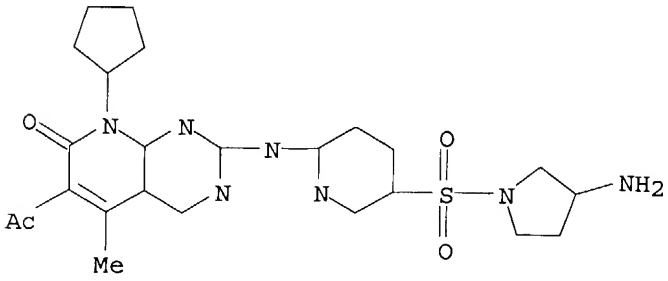
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-32-0 HCAPLUS
CN Piperazine, 1-[[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-5-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]sulfonyl]- (9CI) (CA INDEX NAME)



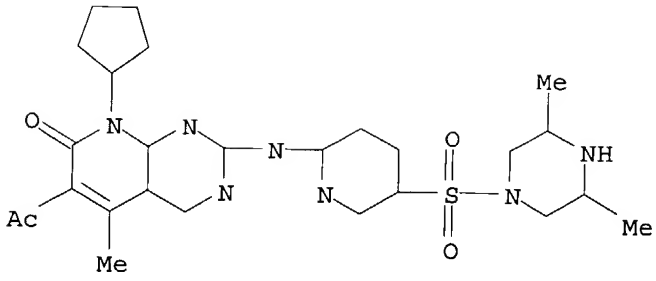
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-33-1 HCAPLUS
CN Morpholine, 4-[[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-5-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]sulfonyl]- (9CI) (CA INDEX NAME)



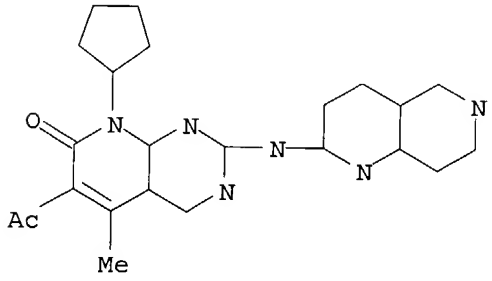
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-34-2 HCAPLUS
CN Pyrrolidine, 1-[[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-5-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]sulfonyl]-3-amino- (9CI) (CA INDEX NAME)



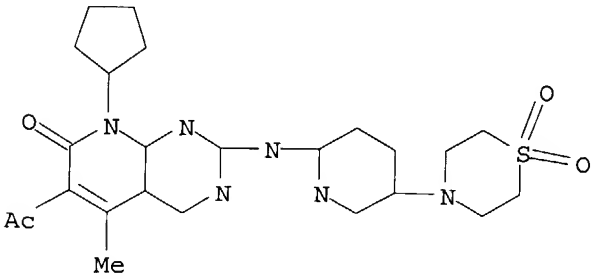
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-35-3 HCAPLUS
CN Piperazine, 1-[[6-[(6-acetyl-8-cyclopentyl-7,8-dihydro-5-methyl-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]-3-pyridinyl]sulfonyl]-3,5-dimethyl- (9CI) (CA INDEX NAME)



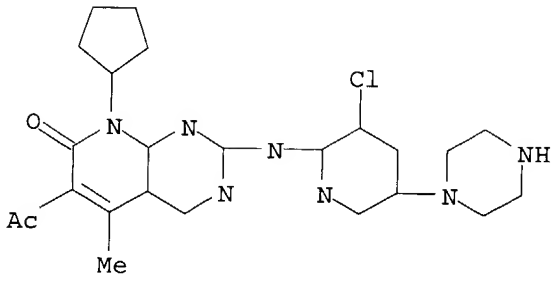
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-36-4 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-5-methyl-2-(1,6-naphthyridin-2-ylamino)- (9CI) (CA INDEX NAME)



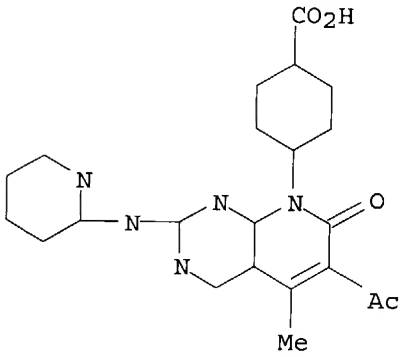
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-37-5 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-8-cyclopentyl-2-[[5-(1,1-dioxido-4-thiomorpholinyl)-2-pyridinyl]amino]-5-methyl- (9CI) (CA INDEX NAME)



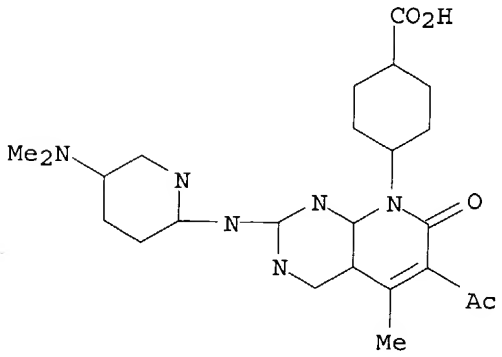
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-39-7 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-2-[[3-chloro-5-(1-piperazinyl)-2-pyridinyl]amino]-8-cyclopentyl-5-methyl- (9CI) (CA INDEX NAME)



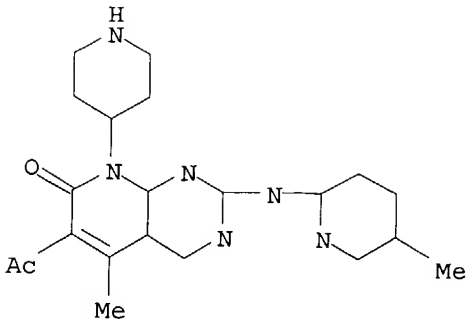
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-40-0 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-[6-acetyl-5-methyl-7-oxo-2-(2-pyridinylamino)pyrido[2,3-d]pyrimidin-8(7H)-yl]- (9CI) (CA INDEX NAME)



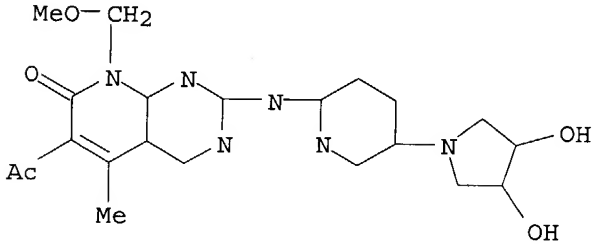
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-41-1 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-[6-acetyl-2-[[5-(dimethylamino)-2-pyridinyl]amino]-5-methyl-7-oxopyrido[2,3-d]pyrimidin-8(7H)-yl]- (9CI) (CA INDEX NAME)



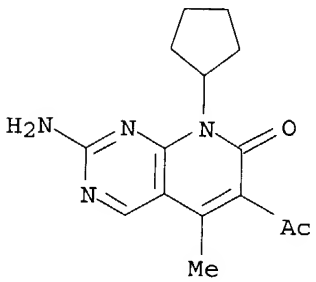
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-51-3 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-5-methyl-2-[(5-methyl-2-pyridinyl)amino]-8-(4-piperidinyl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 571192-52-4 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-2-[[5-(3,4-dihydroxy-1-pyrrolidinyl)-2-pyridinyl]amino]-8-(methoxymethyl)-5-methyl- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
IT **571189-64-5P**, 6-Acetyl-2-amino-8-cyclopentyl-5-methyl-8H-pyrido[2,3-d]pyrimidin-7-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrido[2,3-d]pyrimidinones as cdk4 inhibitors for treating cell proliferative disorders)
RN 571189-64-5 HCAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 6-acetyl-2-amino-8-cyclopentyl-5-methyl- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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